

	L #	Hits	Search Text	DBs	Time Stamp
1	L1	319	2f7 or 2d1 or 5h6	USPA T	2003/01/17 13:41
2	L2	1907	530/387.1,388.1.ccls.	USPA T	2003/01/17 13:42
3	L3	10	1 and 2	USPA T	2003/01/17 13:44
4	L4	6	inositolphosphoglycan	USPA T	2003/01/17 13:44

L9 ANSWER 1 OF 83 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:937303 CAPLUS

DOCUMENT NUMBER: 138:20443

TITLE: Endocrine disruptor screening using DNA chips of
endocrine disruptor-responsive genesINVENTOR(S): Kondo, Akihiro; Takeda, Takeshi; Mizutani, Shigetoshi;
Tsujimoto, Yoshimasa; Takashima, Ryokichi; Enoki,
Yuki; Kato, Ikunoshin

PATENT ASSIGNEE(S): Takara Bio Inc., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 386 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002355079	A2	20021210	JP 2002-69354	20020313
PRIORITY APPLN. INFO.: JP 2001-73183 A 20010314				
JP 2001-74993 A 20010315				
JP 2001-102519 A 20010330				

AB A method and kit for detecting endocrine-disrupting chems. using DNA microarrays are claimed. The method comprises prepg. a nucleic acid sample contg. mRNAs or cDNAs originating in cells, tissues, or organisms which have been brought into contact with a sample contg. the endocrine disruptor. The nucleic acid sample is hybridized with DNA microarrays having genes affected by the endocrine disruptor or DNA fragments originating in these genes have been fixed. The results obtained are then compared with the results obtained with the control sample to select the gene affected by the endocrine disruptor. Genes whose expression is altered by tri-Bu tin, 4-octaphenol, 4-nonylphenol, di-N-Bu phthalate, dichlorohexyl phthalate, octachlorostyrene, benzophenone, diethylhexyl phthalate, diethylstilbestrol (DES), and 17-beta. estradiol (E2), were found in mice by DNA chip anal.

L9 ANSWER 2 OF 83 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:772391 CAPLUS

DOCUMENT NUMBER: 137:258588

TITLE: cDNA and protein sequence of a novel human protein
9.46 and their uses in drug screening, diagnosis and
therapeutics

INVENTOR(S): Mao, Yumin; Xie, Yi

PATENT ASSIGNEE(S): Bode Gene Development Co., Ltd., Shanghai, Peop. Rep.
China

SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 36 pp.

CODEN: CNXXEV

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1331197	A	20020116	CN 2000-116903	20000630
PRIORITY APPLN. INFO.: CN 2000-116903 20000630				

AB This invention provides the cDNA and protein sequence of a novel human protein 9.46 cloned from fetal brain. The mol. wt. of protein 9.46 is 9.46 kDa detd. in SDS PAGE and the gene distribution pattern for protein 9.46 is similar to that for G protein .gamma. subunit. The invention discloses the process of screening the agonist and antagonist against the polypeptide. The protein 9.46 can be used to diagnosis and treatment for many diseases such as cAMP and phosphatidyl ***myoinositol*** channel assocd. diseases.

L9 ANSWER 3 OF 83 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 1

ACCESSION NUMBER: 2002101047 EMBASE

TITLE: Expression of cyclin D1/2 in the lungs of strain A/J mice fed chemopreventive agents.
 AUTHOR: Witschi H.; Espiritu I.; Suffia M.; Pinkerton K.E.
 CORPORATE SOURCE: H. Witschi, Ctr. for Health and the Environment, Department of Molecular Biosciences, University of California, One Shields Avenue, Davis, CA 95616, United States.
 hrwitschi@ucdavis.edu
 SOURCE: Carcinogenesis, (2002) 23/2 (289-294).
 Refs: 44
 ISSN: 0143-3334 CODEN: CRNGDP
 COUNTRY: United Kingdom
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
 016 Cancer
 029 Clinical Biochemistry
 037 Drug Literature Index
 LANGUAGE: English
 SUMMARY LANGUAGE: English

AB Male strain A mice were fed a diet containing chemopreventive agents. After 1 and 3 weeks on the diets, lung nuclear fractions were examined for expression of cyclin D1/2 with western blot analysis. In animals fed a diet containing a mixture of ***myoinositol*** and dexamethasone, a treatment found previously to be effective in preventing the development of tobacco smoke-induced lung tumors in A/J mice, cyclin D1/2 expression was reduced to 30-40% of control levels. A similar decrease in cyclin D1/2 expression was found when animals were fed either ***myoinositol*** or dexamethasone alone. Paradoxically, tobacco smoke by itself had a similar effect on cyclin D1/2 expression. On the other hand, several agents that had been previously found not to be effective against tobacco smoke carcinogenesis [phenethyl isothiocyanate, 1,4-phenylenebis(methylene)selenoisocyanate, N-acetylcysteine, acetylsalicylic acid, D-limonene and beta carotene] did not decrease cyclin D1/2 expression after 1 or 3 weeks of feeding. It was concluded that expression of cyclin D1/2 might be a potentially useful marker in the identification of chemopreventive agents for tobacco smoke and could be of some help in the evaluation of their effects.

L9 ANSWER 4 OF 83 MEDLINE DUPLICATE 2
 ACCESSION NUMBER: 2002187187 MEDLINE
 DOCUMENT NUMBER: 21916742 PubMed ID: 11918982
 TITLE: Astroblastoma: diffusion MRI, and proton MR spectroscopy.
 AUTHOR: Sener R N
 CORPORATE SOURCE: Department of Radiology, Ege University Hospital, Bornova, 35100 Izmir, Turkey.. rnsener@hotmail.com
 SOURCE: COMPUTERIZED MEDICAL IMAGING AND GRAPHICS, (2002 May-Jun) 26 (3) 187-91.
 Journal code: 8806104. ISSN: 0895-6111.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200206
 ENTRY DATE: Entered STN: 20020403
 Last Updated on STN: 20020615
 Entered Medline: 20020614

AB A patient with grade II astroblastoma is reported. The ***tumor*** revealed an inhomogenous enhancement pattern on T1-weighted images after contrast medium. It contained cyst-like structures with high signal in FLAIR images, consistent with presence of viscous material. In spectroscopy, NAA was decreased, and Cho was increased. Peaks belonging to lipids and a combined broad peak belonging to ***myoinositol*** and glycine were noticed. In diffusion MRI, the mean apparent diffusion coefficient (ADC) value of intratumoral cyst-like structures was $2.12 \times 10^{-3} \text{ mm}^2/\text{s}$ less than that of CSF. The matrix of the ***tumor*** had lower ADC values ranging from 1.19 to $1.25 \times 10^{-3} \text{ mm}^2/\text{s}$, higher than that of normal cerebral parenchyma.

L9 ANSWER 5 OF 83 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2002251931 EMBASE

TITLE: Identification of myo-inositol 1,2-cyclic monophosphate by electrospray tandem mass spectrometry, a major constituent of EGF-stimulated phosphoinositide turnover in MDA 468 cells.

AUTHOR: Mandal S.; Richardson V.J.; Banoub J.; Church J.G.

CORPORATE SOURCE: J.G. Church, Terry Fox Can. Research Laboratories, Faculty of Medicine, Memorial University of Newfoundland, St. John's, Nfld. A1B 3V6, Canada. jchurch@mun.ca

SOURCE: Experimental Cell Research, (2002) 277/2 (131-138).

Refs: 43

ISSN: 0014-4827 CODEN: ECREAL

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 016 Cancer

029 Clinical Biochemistry

037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Epidermal growth factor (EGF) caused an increase in phosphoinositide (PI) turnover in MDA 468 cells. This EGF-stimulated effect was inhibited by the protein tyrosine kinase inhibitor lavendustin A (LA). MDA 468 cells generated an atypical PI turnover profile. Examination and quantitation of the PI metabolite profile showed that even control cells produced a metabolite which was acid-labile and which formed about 60% of the total PI metabolites. By using the technique of electrospray ionization tandem mass spectrometry, we were able to confirm the identity of this acid-labile metabolite through the specific fragmentation as compared with the standard. The precursor molecule fragmented into two distinct productions with molar masses identical to that of the standard myo-inositol 1,2-cyclic monophosphate (cInsP). Changes in the PI turnover profile could be accounted for by the alterations in myo-inositol 1,2-cyclic monophosphate generated in these cells. We thus conclude that, by some as-yet-unidentified mechanism, cyclic inositol monophosphate forms a major constituent of EGF-stimulated PI turnover in MDA 468 cells. .COPYRG. 2002 Elsevier Science (USA).

L9 ANSWER 6 OF 83 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:629742 CAPLUS

DOCUMENT NUMBER: 135:329830

TITLE: Estrogen receptor status in breast ***cancer*** is associated with remarkably distinct gene expression patterns

AUTHOR(S): Gruvberger, Sofia; Ringner, Markus; Chen, Yidong; Panavally, Sujatha; Saal, Lao H.; Borg, Ake; Ferno, Marten; Peterson, Carsten; Meltzer, Paul S.

CORPORATE SOURCE: Department of Oncology, Lund University, Lund, SE-221 00, Swed.

SOURCE: Cancer Research (2001), 61(16), 5979-5984

CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB To investigate the phenotype assocd. with estrogen receptor .alpha. (ER) expression in breast carcinoma, gene expression profiles of 58 node-neg. breast carcinomas discordant for ER status were detd. using DNA microarray technol. Using artificial neural networks as well as std. hierarchical clustering techniques, the tumors could be classified according to ER status, and a list of genes which discriminate tumors according to ER status was generated. The artificial neural networks could accurately predict ER status even when excluding top discriminator genes, including ER itself. By ref. to the serial anal. of gene expression database, we found that only a small proportion of the 100 most important ER discriminator genes were also regulated by estradiol in MCF-7 cells. The results provide evidence that ER+ and ER- tumors display remarkably different gene-expression phenotypes not solely explained by differences

in estrogen responsiveness.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 83 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2001039288 EMBASE

TITLE: 3-deoxy-3-substituted-D-myo-inositol imidazolyl ether lipid phosphates and carbonate as inhibitors of the phosphatidylinositol 3-kinase pathway and ***cancer*** cell growth.

AUTHOR: Hu Y.; Meuillet E.J.; Berggren M.; Powis G.; Kozikowski A.P.

CORPORATE SOURCE: A.P. Kozikowski, Drug Discovery Program, Department of Neurology, Georgetown University Medical Center, 3900 Reservoir Road NW, Washington, DC 20007, United States. kozikowa@giccs.georgetown.edu

SOURCE: Bioorganic and Medicinal Chemistry Letters, (22 Jan 2001) 11/2 (173-176). Refs: 33

ISSN: 0960-894X CODEN: BMCLE8

PUBLISHER IDENT.: S 0960-894X(00)00640-5

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 016 Cancer

030 Pharmacology

037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

AB 3-Modified D-myo-inositol imidazolyl ether lipid phosphates and a carbonate were synthesized and evaluated as inhibitors of PI3-K and Akt. These data are presented along with IC(50) values for the inhibition of the growth of three ***cancer*** cell lines. .COPYRGT. 2001 Elsevier Science Ltd.

L9 ANSWER 8 OF 83 MEDLINE DUPLICATE 3

ACCESSION NUMBER: 2001093398 MEDLINE

DOCUMENT NUMBER: 21023398 PubMed ID: 11147898

TITLE: Magnetic resonance spectroscopy of brain hemangiopericytomas: high ***myoinositol*** concentrations and discrimination from meningiomas.

AUTHOR: Barba I; Moreno A; Martinez-Perez I; Tate A R; Cabanas M E; Baquero M; Capdevila A; Arus C

CORPORATE SOURCE: Departament de Bioquímica i Biologia Molecular, Universitat Autònoma de Barcelona, Cerdanyola del Valles, Spain.

SOURCE: JOURNAL OF NEUROSURGERY, (2001 Jan) 94 (1) 55-60. Journal code: 0253357. ISSN: 0022-3085.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 200101

ENTRY DATE: Entered STN: 20010322

Last Updated on STN: 20010322

Entered Medline: 20010125

AB OBJECT: Hemangiopericytomas are a rare type of brain ***tumor*** that are very similar to meningiomas in appearance and symptoms but require different treatment. It is not normally possible to distinguish between them by using magnetic resonance (MR) imaging and computerized tomography studies. However, discrimination may be possible by using in vivo MR spectroscopy (MRS) because the biochemical composition of these two lesions is different. The goal of this study was to describe the use of MRS in discriminating between these similar ***tumor*** types. METHODS: In vivo MRS spectra were acquired in 27 patients (three with hemangiopericytomas and 24 with meningiomas) by using a single-voxel proton brain examination system at 1.5 teslas with short- (20-msec) and long- (135-msec) echo times. In addition, brain biopsy specimens obtained by open craniotomy were frozen within 5 minutes of resection and stored in

liquid nitrogen until they were used. The specimens were powdered, extracted with perchloric acid, redissolved in 2H₂O₂ and high-resolution in vitro MRS was used at 9.4 teslas to record their spectra. CONCLUSIONS: In this study the authors show that hemangiopericytomas could be clearly distinguished from meningiomas because they have a larger peak at 3.56 ppm. Measurements of extracts of the tumors and comparison of spectra acquired with MRS at long- (135-msec) and short- (20-msec) echo times established that this was due to the much higher levels of ***myoinositol*** in the hemangiopericytomas.

L9 ANSWER 9 OF 83 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
 ACCESSION NUMBER: 2001321405 EMBASE
 TITLE: [How and why maternal metabolic disturbance affects embryonic development].
 COMMENT ET POURQUOI L'EQUILIBRE METABOLIQUE DE LA MERE AFFECTE-T-IL L'EMBRYON?
 AUTHOR: Fontaine P.
 CORPORATE SOURCE: P. Fontaine, C.H.R.U. Clinique Marc Linquette, Service d'Endocrino-Diabetologie, Rue du Professeur Laguesse, 59037 LILLE CEDEX, France. p-fontaine@chru-lille.fr
 SOURCE: Diabetes and Metabolism, (2001) 27/4 II (3S13-3S18).
 Refs: 42
 ISSN: 1262-3636 CODEN: DIMEFW
 COUNTRY: France
 DOCUMENT TYPE: Journal; Conference Article
 FILE SEGMENT: 003 Endocrinology
 010 Obstetrics and Gynecology
 017 Public Health, Social Medicine and Epidemiology
 021 Developmental Biology and Teratology
 LANGUAGE: French
 SUMMARY LANGUAGE: English; French

AB Prevalence of congenital malformations in infants born to women with diabetes mellitus remains high (between 6 and 10 %), which is between 3 and 5 times higher than in the general population. Major congenital anomalies are 7 to 10 times more frequent in infants born to diabetics. Normal pregnancy is a state of metabolic stress that requires a high degree of maternal physiological adaptation to help optimize fetal growth. Decreased insulin sensitivity throughout pregnancy with reactional hyperinsulinism helps metabolic efficiency. Changes are observed in glucose, lipid and protein metabolism during pregnancy with a rapid switch from anabolism to catabolism. Diabetic women have absolute or relative insulin deficiency and display abnormalities in carbohydrate, lipid and protein metabolism. These abnormalities can adversely affect embryo growth and explain the high prevalence of spontaneous abortions and congenital malformations. There is a multifactorial origin, of which hyperglycemia in early embryo development is the most important. Hyperglycemia-induced malformations are mediated by sorbital accumulation, arachidonic acid and ***myoinositol*** deficiencies and high concentrations of .beta.-hydroxybutyrate. Accumulation of free oxygen radicals by increased formation and decreased clearance may serve as metabolic common denominators for teratogenic processes. Other factors such as zinc deficiency, the presence of somatomedin inhibitors and released TNF.alpha. are candidates. Human clinical studies are not consistent with a genetic predisposition to diabetes-related malformations. Progress is needed in pre-conception care of diabetes and blood glucose must be strictly controlled during early pregnancy.

L9 ANSWER 10 OF 83 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2000:457304 CAPLUS
 DOCUMENT NUMBER: 133:55669
 TITLE: Treatment and diagnosis of ***cancer*** using inositolphosphoglycans antagonists
 INVENTOR(S): Rademacher, Thomas William; Caro, Hugo
 PATENT ASSIGNEE(S): Rademacher Group Limited, UK
 SOURCE: PCT Int. Appl., 48 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent

LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000039589	A1	20000706	WO 1999-GB4382	19991223
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1141723	A1	20011010	EP 1999-962426	19991223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002533475	T2	20021008	JP 2000-591437	19991223
PRIORITY APPLN. INFO.: GB 1998-28564 A 19981223				
WO 1999-GB4382 W 19991223				

AB Inositolphosphoglycans (IPGs), and in particular A-type substances comprising myo-inositol, are ***tumor*** autocrine factors (TAFs), that is factors which cause ***tumor*** cell proliferation. The use of A-type IPG antagonists for the treatment of ***cancer*** and a method for the diagnosis or prognosis of ***cancer*** based on the presence or amt. of IPGs in a sample from a patient is disclosed.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 11 OF 83 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:830401 CAPLUS

DOCUMENT NUMBER: 134:512

TITLE: Method of treating angiogenesis in ***tumor*** tissue with a inositol trisphosphate

INVENTOR(S): Siren, Matti

PATENT ASSIGNEE(S): Perstorp AB, Swed.

SOURCE: U.S., 7 pp., Cont.-in-part of U.S. Ser. No. 860,511, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6153603	A	20001128	US 1998-93074	19980522
PRIORITY APPLN. INFO.: US 1997-860511 B2 19970627				

AB The present invention relates to a method of treating angiogenesis in ***tumor*** tissue, such as glioma and glioblastoma tissue. The method comprises administering to a mammal, including, man an effective amt. at an isomer of inositol trisphosphate, such as D-myo-inositol-1,2,6-trisphosphate, or a pharmaceutically acceptable salt thereof.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 12 OF 83 MEDLINE DUPLICATE 4

ACCESSION NUMBER: 2000247098 MEDLINE

DOCUMENT NUMBER: 20247098 PubMed ID: 10783321

TITLE: Chemoprevention of tobacco-smoke lung carcinogenesis in mice after cessation of smoke exposure.

AUTHOR: Witschi H; Uyeminami D; Moran D; Espiritu I

CORPORATE SOURCE: Institute of Toxicology and Environmental Health and Department of Molecular Biosciences, School of Veterinary Medicine, University of California, One Shields Avenue,

Davis, CA 95616, USA.. hrwitschi@ucdavis.edu

CONTRACT NUMBER: 1S10-RR04759 (NCRR)

ES05707 (NIEHS)

ES07908 (NIEHS)

+

SOURCE: CARCINOGENESIS, (2000 May) 21 (5) 977-82.

Journal code: 8008055. ISSN: 0143-3334.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200006

ENTRY DATE: Entered STN: 20000622

Last Updated on STN: 20000622

Entered Medline: 20000615

AB Male strain A/J mice were exposed for 6 h per day, 5 days per week to a mixture of 89% cigarette sidestream smoke and 11% mainstream smoke. Total suspended particulate concentrations were 137 mg/m(3). In experiment 1, animals were exposed for 5 months to tobacco smoke and given a 4 month recovery period in air. Lung ***tumor*** multiplicity was 2.4 and incidence 89%. Animals exposed to filtered air had 1.0 ***tumor*** per lung (65% incidence). In animals kept for 5 months in smoke, removed into air and then fed a diet containing a mixture of ***myoinositol*** and dexamethasone, ***tumor*** multiplicity was 1.0 and incidence was 62%. These values were significantly ($P < 0.01$) lower than in animals exposed to smoke and identical to values seen in controls. In animals fed a diet containing 250 mg/kg each of phenethyl isothiocyanate and benzyl isothiocyanate during the entire 9 months, lung ***tumor*** multiplicity was 2.1 and incidence 96%, not significantly different from animals exposed to smoke and fed control diet. In experiment 2, animals were exposed for 5 months to smoke, followed by a 4 month recovery period in air and were fed during the entire period a diet containing either D-limonene or 1, 4-phenylenebis(methylene)selenoisocyanate (p-XSC). In animals exposed to tobacco smoke and fed control diet, lung ***tumor*** multiplicity was 2.8, whereas in the animals fed D-limonene it was 2.6 and in the animals fed p-XSC it was 2.4. The differences to the controls were statistically not significant. It was concluded that ***myoinositol***-dexamethasone successfully prevents the development of tobacco smoke-induced lung tumors even if administered when the animals have 'quit' smoking. On the other hand, agents otherwise shown to prevent lung ***tumor*** formation following administration of 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone or benzo[a]pyrene were ineffective against tobacco smoke.

L9 ANSWER 13 OF 83 MEDLINE DUPLICATE 5

ACCESSION NUMBER: 2000168620 MEDLINE

DOCUMENT NUMBER: 20168620 PubMed ID: 10706103

TITLE: A germ-line p53 mutation accelerates pulmonary tumorigenesis: p53-independent efficacy of chemopreventive agents green tea or dexamethasone/myo-inositol and chemotherapeutic agents taxol or adriamycin.

AUTHOR: Zhang Z; Liu Q; Lantry L E; Wang Y; Kelloff G J; Anderson M W; Wiseman R W; Lubet R A; You M

CORPORATE SOURCE: Department of Pathology, Medical College of Ohio, Toledo 43699, USA.

CONTRACT NUMBER: CA58554 (NCI)

CA78797 (NCI)

CN65111 (NCI)

SOURCE: CANCER RESEARCH, (2000 Feb 15) 60 (4) 901-7.

Journal code: 2984705R. ISSN: 0008-5472.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200003

ENTRY DATE: Entered STN: 20000330

Last Updated on STN: 20000330

Entered Medline: 20000320

AB Recent evidence indicates that individuals with a p53 germ-line mutation (Li-Fraumeni syndrome) have a 50% risk of developing lung ***cancer*** by age 60. In this study, p53 heterozygous knockout mice and p53 transgenic mice carrying a dominant negative mutant were crossed with the A/J mouse, which is highly susceptible to lung ***tumor*** induction, to investigate whether a p53 germ-line mutation is a predisposing gene for carcinogen-induced pulmonary adenomas in mice. The number of lung tumors was not significantly increased in (TSG-p53 x A/J)F1 p53 heterozygous knockout mice as compared with that in (TSG-p53 x A/J)F1 wt mice 16 weeks after exposure to N-nitrosomethylurea (MNU). In contrast, an average of 22 lung tumors were observed in (UL53-3 x A/J)F1 mice carrying a mutant p53 transgene (135Valp53) compared with an average of 7 lung tumors seen in (UL53-3 x A/J)F1 wt mice after treatment with N-nitrosomethylurea. Similar enhancement of lung ***tumor*** multiplicity (approximately 3-fold) was seen when mutant versus wt mice were treated with the tobacco-related carcinogens benzo[a]pyrene or 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone. These results suggest that the mutant p53 transgene may have a dominant negative effect on the wt p53. The potential usefulness of this new mouse model in lung ***cancer*** chemoprevention and chemotherapy was examined. The chemopreventive efficacy of the green tea or a combination of dietary dexamethasone and ***myoinositol*** and the chemotherapeutic efficacy of Taxol or Adriamycin was examined in wt mice or mice with a mutation in the p53 gene. Mice treated with dexamethasone/myo-inositol and green tea displayed an average of 70 and 50% inhibition of lung tumors, respectively, regardless of p53 status. Similarly, when mice bearing established lung adenomas were treated with Taxol or Adriamycin, a decrease in ***tumor*** volume of approximately 70% was observed independent of p53 mutation status. Thus, the (UL53-3 x A/J)F1 p53 transgenic mouse seems to be an excellent model for human carriers of p53 germ-line mutations (Li-Fraumeni syndrome). Furthermore, the lung adenomas generated in this model possess mutations in both the K-ras proto-oncogene and the p53 ***tumor*** suppressor gene. This model should prove directly useful for chemoprevention and chemotherapy studies.

L9 ANSWER 14 OF 83 MEDLINE

ACCESSION NUMBER: 2001139209 MEDLINE

DOCUMENT NUMBER: 21038166 PubMed ID: 11195468

TITLE: Successful and not so successful chemoprevention of tobacco smoke-induced lung tumors.

AUTHOR: Witschi H

CORPORATE SOURCE: ITEH and Department of Molecular Biosciences, School of Veterinary Medicine, University of California, One Shields Avenue, Davis, CA 95616, USA.. hrwitschi@ucdavis.edu

CONTRACT NUMBER: ES05707 (NIEHS)

ES07499 (NIEHS)

ES07908 (NIEHS)

SOURCE: EXPERIMENTAL LUNG RESEARCH, (2000 Dec) 26 (8) 743-55.

Journal code: 8004944. ISSN: 0190-2148.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200103

ENTRY DATE: Entered STN: 20010404

Last Updated on STN: 20010905

Entered Medline: 20010308

AB Strain A/J mice underwent whole body exposure for 6 hours a day, 5 days a week, for 5 months to a mixture of cigarette sidestream and mainstream smoke (89%-11%; total suspended particulates 80-150 mg/m3), then were kept for another 4 months in air before being killed for scoring of lung tumors. In 7 independent experiments, lung ***tumor*** multiplicity was significantly increased in all 7 trials and lung ***tumor*** incidence in 5. When animals were kept for 9 months in smoke, lung ***tumor*** multiplicity was not significantly higher than in controls, although lung ***tumor*** incidence was. The following chemopreventive

agents were evaluated: green tea, phenethyl isothiocyanate (PEITC), acetylsalicylic acid (ASA), N-acetylcysteine (NAC), p-XSC (1,4-phenylenebis[methylene]selenocyanate), d-limonene (DL), and a mixture of PEITC and BITC (benzyl isothiocyanate). In animals exposed to tobacco smoke, none of these agents reduced lung ***tumor*** multiplicity or incidence. As a control, the effects of the same agents were examined in A/J mice initiated with 4-(methylnitrosamino)-1-(3pyridyl)-1-butanone (NNK) or urethane. In mice injected with NNK, green tea and ASA did not reduce lung ***tumor*** multiplicities and NAC had no effect on urethane-induced lung tumors, whereas PEITC, p-XSC and DL reduced NNK-induced ***tumor*** multiplicities to 20% to 50% of control values. On the other hand, dietary mixture of ***myoinositol*** and dexamethasone was not only highly protective against NNK, but reduced lung ***tumor*** multiplicities and incidence in smoke-exposed animals to control values. This effect was also seen when the animals were fed the myo-inositol-dexamethasone mixture once they were removed from smoke. It is concluded that in animal studies it might be preferable to evaluate the effectiveness of putative chemopreventive agents against full tobacco smoke rather than against selected model compounds. The observations made with myo-inositol-dexamethasone suggest that people who have recently quit smoking might benefit the most from active chemoprevention.

L9 ANSWER 15 OF 83 MEDLINE DUPLICATE 6
 ACCESSION NUMBER: 2001269799 MEDLINE
 DOCUMENT NUMBER: 21150529 PubMed ID: 11251398
 TITLE: In vivo proton magnetic resonance spectroscopy of brain tumors.
 AUTHOR: Fountas K N; Kapsalaki E Z; Gotsis S D; Kapsalakis J Z; Smisson H F 3rd; Johnston K W; Robinson J S Jr; Papadakis N
 CORPORATE SOURCE: Department of Neurosurgery, Medical Center of Central Georgia, Macon, Ga., USA.. knfountas@mailexcite.com
 SOURCE: STEREOTACTIC AND FUNCTIONAL NEUROSURGERY, (2000) 74 (2) 83-94.
 Journal code: 8902881. ISSN: 1011-6125.
 PUB. COUNTRY: Switzerland
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200105
 ENTRY DATE: Entered STN: 20010529
 Last Updated on STN: 20010529
 Entered Medline: 20010521

AB The ability of magnetic resonance spectroscopy (MRS) to differentiate neoplastic brain cells and their metabolic and structural characteristics is evaluated. We examined 120 patients with brain tumors using a 1.5-tesla MRI unit and MRS. The peak areas of N-acetyl-aspartate (NAA), phosphocreatine-creatine (Pcr-Cr), choline-containing compounds (Cho), lactate, lipids, ***myoinositol***, amino acids and the ratios of NAA/Pcr-Cr, NAA/Cho and Cho/Pcr-Cr were calculated by a standard integral algorithm. In normal brain tissue, the following metabolites were identified: NAA at 2.0 ppm, Pcr-Cr at 3.0 ppm and Cho at 3.2 ppm. The different concentrations of the metabolites examined and their role in the biochemical profile of different types of tumors are discussed. The confidence interval of the MRS versus pathology was between 0.9 and 0.954, while it was between 0.52 and 0.631 for MRI versus pathology. The Cho/Pcr-Cr ratio is a very important malignancy marker for histologic ***tumor*** grading of astrocytomas. The greater this ratio, the higher the grade of the astrocytoma. NAA/Pcr-Cr together with Cho/Pcr-Cr help specify the presence or absence of a neoplasm. Proton MRS is a useful and promising diagnostic modality not only in diagnosing but also in grading solid brain tumors.

L9 ANSWER 16 OF 83 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2000:166948 CAPLUS
 DOCUMENT NUMBER: 133:37847
 TITLE: Effects and clinical significance of vincristine on pentagastrin-stimulated proliferation of human colonic

cancer cell line SW480

AUTHOR(S): Xie, Bin; He, Suang-wu; Wang, Dai-ke
 CORPORATE SOURCE: Daping Hospital, Third Military Med. Univ., Chungking,
 400042, Peop. Rep. China

SOURCE: Zhongguo Puwai Jichu Yu Linchuang Zazhi (2000), 7(1),
 3-5

CODEN: ZJLZFX; ISSN: 1007-9424

PUBLISHER: Zhongguo Puwai Jichu Yu Linchuang Zazhi Bianji
 Weiyuanhui

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB Vincristine lowered the viable cell count of human colon ***cancer***
 SW480 cells stimulated with pentagastrin. It also lowered the concns. of
 myoinositol triphosphate and intracellular Ca^{2+} and the activity
 of protein kinase C. The effects of vincristine may be mediated by the
 phosphoinositide signaling pathway. This provides exptl. evidence for
 antineoplastic therapy in patients with colon ***cancer***.

L9 ANSWER 17 OF 83 MEDLINE

ACCESSION NUMBER: 2000020260 MEDLINE

DOCUMENT NUMBER: 20020260 PubMed ID: 10551852

TITLE: Role of the inositol 1,4,5-trisphosphate receptor in Ca^{2+}
 feedback inhibition of calcium release-activated calcium
 current ($I_{(crac)}$).

AUTHOR: Broad L M; Armstrong D L; Putney J W Jr

CORPORATE SOURCE: Laboratory of Signal Transduction, NIEHS, National
 Institutes of Health, Research Triangle Park, North
 Carolina 27709, USA.. broad@niehs.nih.gov

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 Nov 12) 274 (46)
 32881-8.

Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200001

ENTRY DATE: Entered STN: 20000114

Last Updated on STN: 20000114

Entered Medline: 20000103

AB We examined the activation and regulation of calcium release-activated
 calcium current ($I_{(crac)}$) in RBL-1 cells in response to various Ca^{2+}
 store-depleting agents. With $[Ca^{2+}]_i$ strongly buffered to 100 nM,
 $I_{(crac)}$ was activated by ionomycin, thapsigargin, inositol
 1,4,5-trisphosphate ($IP(3)$), and two metabolically stable $IP(3)$ receptor
 agonists, adenophostin A and L-alpha-glycerophospho-D- ***myoinositol***
 -4,5-bisphosphate (GPIP(2)). With minimal $[Ca^{2+}]_i$ buffering, with
 $[Ca^{2+}]_i$ free to fluctuate $I_{(crac)}$ was activated by ionomycin,
 thapsigargin, and by the potent $IP(3)$ receptor agonist, adenophostin A,
 but not by GPIP(2) or $IP(3)$ itself. Likewise, when $[Ca^{2+}]_i$ was
 strongly buffered to 500 nM, ionomycin, thapsigargin, and adenophostin A
 did and GPIP(2) and $IP(3)$ did not activate detectable $I_{(crac)}$. However,
 with minimal $[Ca^{2+}]_i$ buffering, or with $[Ca^{2+}]_i$ buffered to 500
 nM, GPIP(2) was able to fully activate detectable $I_{(crac)}$ if uptake of
 Ca^{2+} intracellular stores was first inhibited. Our findings suggest that
 when $IP(3)$ activates the $IP(3)$ receptor, the resulting influx of Ca^{2+}
 quickly inactivates the receptor, and Ca^{2+} is re-accumulated at sites
 that regulate $I_{(crac)}$. Adenophostin A, by virtue of its high receptor
 affinity, is resistant to this inactivation. Comparison of
 thapsigargin-releasable Ca^{2+} pools following activation by different
 $IP(3)$ receptor agonists indicates that the critical regulatory pool of
 Ca^{2+} may be very small in comparison to the total $IP(3)$ -sensitive
 component of the endoplasmic reticulum. These findings reveal new and
 important roles for $IP(3)$ receptors located on discrete $IP(3)$ -sensitive
 Ca^{2+} pools in calcium feedback regulation of $I_{(crac)}$ and capacitative
 calcium entry.

L9 ANSWER 18 OF 83 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:4336 CAPLUS

DOCUMENT NUMBER: 132:333813

TITLE: Suppression of lung and liver carcinogenesis in mice
by oral administration of myo-inositolAUTHOR(S): Nishino, Hoyoku; Murakoshi, Michiaki; Masuda,
Mitsuharu; Tokuda, Harukuni; Satomi, Yoshiko; Onozuka,
Mari; Yamaguchi, Shino; Bu, Ping; Tsuruta, Atsushi;
Nosaka, Kazuto; Baba, Masaki; Takasuka, NobuoCORPORATE SOURCE: Department of Biochemistry, Kyoto Prefectural
University of Medicine, Kyoto, 602-8566, Japan

SOURCE: Anticancer Research (1999), 19(5A), 3663-3664

CODEN: ANTRD4; ISSN: 0250-7005

PUBLISHER: International Institute of Anticancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Myo-inositol can inhibit carcinogenesis in various organs, such as the mammary gland, colon, and lung. The inhibitory effects of myo-inositol on lung and liver carcinogenesis were studied in male C3H/He mice having a high rate of spontaneous liver carcinogenesis. Myo-inositol was added to the drinking water at 1%. The antitumor effects of myo-inositol on lung carcinogenesis were confirmed. Significant suppression of liver carcinogenesis was obsd. in mice treated for 40 wk. In the control group without myo-inositol, 88% animals developed liver tumors, whereas in the myo-inositol group the incidence was 38%. The av. no. of liver tumors per mouse was also decreased by myo-inositol from 7.8 in controls to 0.8 in the myo-inositol group. Thus, myo-inositol may be useful for

cancer chemoprevention in the liver and lung.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 19 OF 83 MEDLINE DUPLICATE 7

ACCESSION NUMBER: 1999360595 MEDLINE

DOCUMENT NUMBER: 99360595 PubMed ID: 10433213

TITLE: Alterations in intracellular messengers mobilized by
gonadotropin-releasing hormone in an experimental ovarian

tumor

AUTHOR: Chamson-Reig A; Pignataro O P; Libertun C; Lux-Lantos V A

CORPORATE SOURCE: Instituto de Biologia y Medicina Experimental-CONICET,
Buenos Aires, Argentina.

SOURCE: ENDOCRINOLOGY, (1999 Aug) 140 (8) 3573-80.

Journal code: 0375040. ISSN: 0013-7227.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 199908

ENTRY DATE: Entered STN: 19990827

Last Updated on STN: 19990827

Entered Medline: 19990817

AB Cells derived from an experimental luteinized ovarian ***tumor*** are more sensitive to GnRH endocrine action than control luteal cells. In an attempt to understand the possible causes of the differential sensibility to GnRH action, we examined the number and affinity of GnRH receptors and the second messenger response to GnRH stimulation in both tissues. For GnRH receptor studies membranes were obtained from 4- to 6-week-old ovarian tumors (luteoma) and ovaries from prepubertal rats treated with 25 IU PMSG and 25 IU hCG (SPO) and were incubated with [¹²⁵I]Buserelin. The number of GnRH receptors were increased in luteoma compared with that in SPO ovaries; dissociation constants were similar in both tissues. GnRH stimulation of second messenger release was assessed in cells obtained from luteoma and SPO ovaries by collagenase treatment. Buserelin (100 ng/ml) induced a significant 35% calcium increase in SPO cells, as determined by the fura-2 method; in luteoma cells no response was observed after buserelin stimulation, although a calcium transient was induced by thapsigargin (0.5 microM), an inhibitor of Ca²⁺-adenosine triphosphatase associated with the endoplasmic reticulum. The effect of buserelin on inositol phosphates was evaluated after incubation of luteoma and SPO

cells with [3H] ***myoinositol*** for 48 h. Buserelin induced a 400% increase in inositol trisphosphate in SPO cells. Again, luteoma cells did not respond to buserelin stimulation, although NaF (10 mM), an activator of G proteins coupled to phospholipase C, induced an 800% increase in inositol trisphosphate. Although the number of GnRH receptors is augmented in luteoma cells, justifying an increased endocrine response, neither inositol phosphates nor intracellular calcium were released by a GnRH analog, indicating the uncoupling of GnRH receptors from phospholipase C. These data provide evidence that the transformation of the ovary into a luteoma implies the acquisition of novel characteristics in the GnRH receptor second messenger-generating system.

L9 ANSWER 20 OF 83 MEDLINE
 ACCESSION NUMBER: 1999231614 MEDLINE
 DOCUMENT NUMBER: 99231614 PubMed ID: 10217262
 TITLE: Neuroprotective role of Na⁺/myo-inositol cotransporter
 against veratridine cytotoxicity.
 AUTHOR: Yamashita T; Yamauchi A; Miyai A; Taniguchi M; Yoshimine T;
 Tohyama M
 CORPORATE SOURCE: Department of Anatomy and Neuroscience, Osaka University
 Medical School Suita, Japan.
 SOURCE: JOURNAL OF NEUROCHEMISTRY, (1999 May) 72 (5) 1864-70.
 Journal code: 2985190R. ISSN: 0022-3042.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199905
 ENTRY DATE: Entered STN: 19990517
 Last Updated on STN: 19990517
 Entered Medline: 19990506

AB Na⁺/myo-inositol cotransporter has been shown to protect cells from the perturbing effects of hypertonic stress by the accumulation of myo-inositol. Here we report a regulatory mechanism for the cotransporter. Induction of myo-inositol cotransporter mRNA was observed after exposure to veratridine, a voltage-gated sodium channel opener. The veratridine-elicited induction was inhibited when Na⁺ was eliminated from the bath, although calcium chelation failed to modify the gene expression. Veratridine evoked an accumulation of Na⁺ in the cells, which paralleled the abundance of the mRNA. These results strongly suggested that an increase in Na⁺ influx due to sodium channel opening affected transcription of the cotransporter gene. Activity of the myo-inositol cotransporter was also up-regulated after veratridine exposure. To clarify the possible roles of ***myoinositol*** accumulation under veratridine exposure, we next examined the neurotoxic effects of veratridine when myo-inositol uptake was blocked. Neither 30 microM veratridine nor 500 microM 2-O,C-methylene myo-inositol, a competitive inhibitor of myo-inositol, elicited apparent cytotoxicity. However, a combination of these agents markedly increased cytotoxicity in culture, suggesting that an adequate amount of myo-inositol was necessary when the cells were stimulated with veratridine.

L9 ANSWER 21 OF 83 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 1999:475224 CAPLUS
 DOCUMENT NUMBER: 131:242494
 TITLE: Chemoprevention of tobacco smoke-induced lung tumors
 in A/J strain mice with dietary myo-inositol and
 dexamethasone
 AUTHOR(S): Witschi, Hanspeter; Espiritu, Imelda; Uyeminami, Dale
 CORPORATE SOURCE: Institute of Toxicology and Environmental Health,
 School of Veterinary Medicine, University of
 California, Davis, CA, 95616, USA
 SOURCE: Carcinogenesis (1999), 20(7), 1375-1378
 CODEN: CRNGDP; ISSN: 0143-3334
 PUBLISHER: Oxford University Press
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Male A/J strain mice were fed AIN-76A diet supplemented with ***myoinositol*** /dexamethasone (10 g and 0.5 mg/kg feed) or acetylsalicylic acid (300 mg/kg) and exposed for 5 mo to a mixt. of sidestream and mainstream cigarette smoke at a concn. of 132 mg total suspended particulates/m³. After the tobacco smoke exposure, the mice were allowed to recover for 4 mo in filtered air. In animals fed the AIN-75A diet alone or with acetylsalicylic acid the av. no. of tumors/lung was 2.1, whereas in animals fed the ***myoinositol*** /dexamethasone diet the av. lung ***tumor*** multiplicity was 1.0. In animals exposed to filtered air the lung ***tumor*** multiplicities were 0.6 in animals fed AIN-76A or ***myoinositol*** /dexamethasone and 1.2 in animals fed acetylsalicylic acid. Thus, the combination of ***myoinositol*** and dexamethasone is an effective chemopreventive regimen against tobacco smoke-induced lung tumorigenesis.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 22 OF 83 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 1999335777 EMBASE

TITLE: Regional age dependence of human brain metabolites from infancy to adulthood as detected by quantitative localized proton MRS.

AUTHOR: Pouwels P.J.W.; Brockmann K.; Kruse B.; Wilken B.; Wick M.; Hanefeld F.; Frahm Y.

CORPORATE SOURCE: Dr. Y. Frahm, Biomedizinische NMR Forschungs GmbH, Max-Planck-Inst. Biophysik. Chemie, D-37070 Gottingen, Germany

SOURCE: Pediatric Research, (1999) 46/4 (474-485).

Refs: 39

ISSN: 0031-3998 CODEN: PEREBL

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 007 Pediatrics and Pediatric Surgery

008 Neurology and Neurosurgery

023 Nuclear Medicine

027 Biophysics, Bioengineering and Medical Instrumentation

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Regional changes of metabolite concentrations during human brain development were assessed by quantitative localized proton magnetic resonance spectroscopy in vivo. Apart from measurements in young healthy adults, the study was based on regional spectra from 97 children who were either healthy or suffered from mental retardation, movement disorders, epilepsies, neoplasm, or vascular malformation. Metabolite quantitation focused on cortical gray and white matter, cerebellum, thalamus, and basal ganglia in six age groups from infancy to adulthood. During infancy and childhood, the concentration of the neuroaxonally located N-acetylaspartate increased in gray matter, cerebellum, and thalamus, whereas a constant level was detected in white matter. These findings are in line with regional differences in the formation of synaptic connections during early development and suggest a role of N-acetylaspartate as a marker of functioning neuroaxonal tissue rather than of the mere presence of nerve cells. This view is further supported by high concentrations of taurine in gray matter and cerebellum during infancy, because taurine is also believed to be involved in the process of synapse formation. Remarkably, in basal ganglia both N-acetylaspartate and taurine remain constant at relatively high concentrations. Other metabolite changes during maturation include increases of N-acetylaspartylglutamate, especially in thalamus and white matter, and a decrease of glutamine in white matter. Despite regional differences and some small changes during the first year of life, the concentrations of creatine, phosphocreatine, choline-containing compounds, ***myoinositol***, and glutamate remain constant afterward. The creatine to phosphocreatine concentration ratio yields 2:1 throughout the human brain irrespective of region or age. The observed increase of the proton resonance line-width with age is most pronounced in basal ganglia and corresponds to the age-related and

tissue-dependent increase of brain iron.

L9 ANSWER 23 OF 83 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:379411 CAPLUS

DOCUMENT NUMBER: 131:168507

TITLE: Role of inositol 1,4,5-trisphosphate and calcium in
gastrin-induced proliferation of human colon cell line
SW480

AUTHOR(S): Xie, Bin; He, Shuangwu

CORPORATE SOURCE: Daping Hospital, Third Military Medical Univ.,
Chungking, 400042, Peop. Rep. China

SOURCE: Di-San Junyi Daxue Xuebao (1999), 21(3), 184-186

CODEN: DYGUE8; ISSN: 1000-5404

PUBLISHER: Di-San Junyi Daxue

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB Objective: To investigate the effects of gastrin on inositol
1,4,5-trisphosphate (IP3) and intracellular calcium (Ca2+) in human colon
cancer cell line SW480 and its role in the proliferation of this
cell line to provide exptl. basis for development of antesignaling therapy
for patients with colon ***cancer***. Methods: 1) Level of IP3 was
analyzed by [3H]- ***myoinositol*** incorporation into inositol
phospholipids in the cells. 2) Level of [Ca2+] was measured by
fluorescence measurement with fura-2/AM, a fluorescent index of (PG)
promoted the levels of IP3 and [Ca2+] and increased VCC of SW480 cells.
2) When proglumide (PGL), a gastrin-receptor antagonist, used in
combination with PG, no significant changes were found in the levels of
IP3 and [Ca2+] and increment of VCC of SW480 cells. Conclusion: Gastrin
might promote the proliferation of SW480 cells through a receptor-mediated
inositol phospholipids signaling pathway.

L9 ANSWER 24 OF 83 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:503329 CAPLUS

DOCUMENT NUMBER: 129:254488

TITLE: 3-Deoxy-D-myo-inositol 1-phosphate, 1-phosphonate, and
ether lipid analogs as inhibitors of
phosphatidylinositol-3-kinase signaling and
cancer cell growth

AUTHOR(S): Qiao, Lixin; Nan, Fajun; Kunkel, Mark; Gallegos,
Alfred; Powis, Garth; Kozikowski, Alan P.

CORPORATE SOURCE: Drug Discovery Program, Georgetown University Medical
Center, Washington, DC, 20007, USA

SOURCE: Journal of Medicinal Chemistry (1998), 41(18),
3303-3306

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The synthesis and the bioactivity of several rationally designed
phosphatidylinositol analogs are presented. The studies have been
directed toward the synthesis of 3-substituted myo-inositol derivs. to
selectively block the effects of myo-inositol-derived second messengers on
cell proliferation and transformation while leaving other aspects of
myo-inositol signalling unaffected. This strategy may offer a basis for
the selective control of ***cancer*** growth without disrupting the
function of normal cells.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 25 OF 83 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1998:406842 BIOSIS

DOCUMENT NUMBER: PREV199800406842

TITLE: Magnetic resonance spectroscopy study of low grade extra
and intracerebral human neoplasms.

AUTHOR(S): Tugnoli, V. (1); Tosi, M. R.; Barbarella, G.; Ricci, R.;
Leonardi, M.; Calbucci, F.; Bertoluzza, A.

CORPORATE SOURCE: (1) Dip. Biochim. 'G. Moruzzi', Univ. Bologna, V. Belmeloro

8/2, 40126 Bologna Italy

SOURCE: Oncology Reports, (Sept.-Oct., 1998) Vol. 5, No. 5, pp.
1199-1203.
ISSN: 1021-335X.

DOCUMENT TYPE: Article

LANGUAGE: English

AB In this study we report an in vitro ¹H magnetic resonance spectroscopy (MRS) characterization of water soluble metabolites obtained from 17 low grade extra and intracerebral human tumors (8 meningiomas, 5 oligodendrogliomas, 2 subependimomas and 2 ependimomas). In addition, the in vivo localized ¹H MRS results for 4 of the meningiomas are reported. The main metabolic features characterizing low grade tumors were investigated. Meningiomas are characterized by high Cho/Cr and Ala/Cr ratios; in many cases both in the in vitro and the in vivo spectra these ratios cannot be evaluated, due to the absence of the Cr metabolite. Low grade oligodendrogliomas are characterized by low Cho/Cr ratios. High amounts of ***myoinositol*** are found in the spectra of ependimomas and subependimomas which are distinguished by different Cho/Cr ratio values and by a different Ala content.

L9 ANSWER 26 OF 83 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:115076 CAPLUS

DOCUMENT NUMBER: 130:332391

TITLE: Anti-carcinogenic effect of isoflavonoids in soybeans

AUTHOR(S): Nishino, Hoyoku

CORPORATE SOURCE: Department of Biochemistry, Kyoto Prefectural University of Medicine, Kyoto, 602-8566, Japan

SOURCE: Daizu Tanpakushitsu Kenkyu (1998), 1, 129-132

CODEN: DTKEFV; ISSN: 1344-4050

PUBLISHER: Fuji Tanpakushitsu Kenkyu Shinko Zaidan

DOCUMENT TYPE: Journal

LANGUAGE: Japanese

AB In the previous study, we showed that genistein, one of the isoflavonoids found in soybean inhibited the proliferation of prostate ***cancer*** DU145 cells. In addn. to prostate ***cancer*** cells, various ***tumor*** cell lines were also proven recently to be sensitive to genistein. In the present study, we found that genistein induced morphol. differentiation, and apoptosis in rat neuroblastoma B104 cells. In the previous study, we showed that oral administration of isoflavonoid-rich soybean hypocotyl powder resulted in suppression of spontaneous liver carcinogenesis in C3H/He male mice. Since various substances in soybean hypocotyl co-existed with isoflavonoids may have anti-carcinogenic activity and/or potentiate the anti-carcinogenic activity of isoflavonoids, studies on these soybean constituents seem to be valuable. In this context, we have started to assess biol. activities of these substances. In the present study, we evaluated the anti-carcinogenic activities of soybean constituent-related compds., i.e., myo-inositol and tocotrienol, and found that these substances were effective to suppress spontaneous liver carcinogenesis in C3H/He male mice, and also 4-nitroquinoline 1-oxide-initiated and glycerol-promoted lung tumorigenesis in ddY male mice.

L9 ANSWER 27 OF 83 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE

8

ACCESSION NUMBER: 1998:115885 BIOSIS

DOCUMENT NUMBER: PREV199800115885

TITLE: Effect of TNF-alpha on SMIT mRNA levels and myo-inositol accumulation in cultured endothelial cells.

AUTHOR(S): Yorek, Mark A. (1); Dunlap, Joyce A.; Thomas, Michael J.; Cammarata, Patrick R.; Zhou, Chen; Lowe, William L., Jr.

CORPORATE SOURCE: (1) 3E17 Veterans Affairs Med. Cent., Iowa City, IA 52246 USA

SOURCE: American Journal of Physiology, (Jan., 1998) Vol. 274, No. 1 PART 1, pp. C58-C71.

ISSN: 0002-9513.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Previously we have shown that hyperosmolarity increases Na⁺-myo-inositol cotransporter (SMIT) activity and mRNA levels in cultured endothelial cells. Because hyperosmolarity and cytokines, such as ***tumor*** necrosis factor-alpha (TNF-alpha), activate similar signal transduction pathways, we examined the effect of TNF-alpha on SMIT mRNA levels and myo-inositol accumulation. In contrast to the effect of hyperosmolarity, TNF-alpha caused a time- and concentration-dependent decrease in SMIT mRNA levels and myo-inositol accumulation. The effect of TNF-alpha on myo-inositol accumulation was found in large-vessel endothelial cells (derived from the aorta and pulmonary artery) and cerebral microvessel endothelial cells. In bovine aorta and bovine pulmonary artery endothelial cells, TNF-alpha activated nuclear factor (NF)-kappaB. TNF-alpha also increased ceramide levels, and C2-ceramide mimicked the effect of TNF-alpha on SMIT mRNA levels and myo-inositol accumulation in bovine aorta endothelial cells. Pyrrolidinedithiocarbamate, genistein, and 7-amino-1-chloro-3-tosylamido-2-heptanone, compounds that can inhibit NF-KB activation, partially prevented the TNF-alpha-induced decrease in myo-inositol accumulation. The effect of TNF-alpha on myo-inositol accumulation was also partially prevented by the protein kinase C inhibitor calphostin C but not by staurosporine. These studies demonstrate that TNF-alpha causes a decrease in SMIT mRNA levels and myo-inositol accumulation in cultured endothelial cells, which may be related to the activation of NF-kappaB.

L9 ANSWER 28 OF 83 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1997:261737 BIOSIS

DOCUMENT NUMBER: PREV199799568340

TITLE: Nuclear accumulation of fibroblast growth factor receptors in human glial cells - association with cell proliferation.

AUTHOR(S): Stachowiak, E. K.; Maher, P. A.; Tucholski, J.; Mordechai, E.; Joy, A.; Moffett, J.; Coons, S.; Stachowiak, M. K. (1)

CORPORATE SOURCE: (1) Barrow Neurol. Inst., Phoenix, AZ 85013 USA

SOURCE: Oncogene, (1997) Vol. 14, No. 18, pp. 2201-2211.

ISSN: 0950-9232.

DOCUMENT TYPE: Article

LANGUAGE: English

AB In this study we describe the presence of high affinity FGF-2 binding sites in the nuclei of U251MG glioma cells (K_d=7 pm). Immunoprecipitation of total cell extracts with FGF receptor (FGFR) 14 antibodies showed that U251MG glioma cells express only FGFR1. (125I)FGF-2 cross linking to nuclear extracts followed by FGFR1 immunoprecipitation showed that FGFR1 may account for the nuclear FGF-2 binding sites. Western blot analysis demonstrated the presence of 103, 118 kDa and small amounts of 145 kDa FGFR1 isoforms in the nuclei of glioma cells. All isoforms contain both the C- and N-terminal domains. Nuclear FGFR1 retains kinase activity. Immunocytochemistry using confocal microscopy showed specific FGFR1 immunoreactivity within the nuclear interior. In continuously proliferating glioma cells, nuclear FGFR1 is constitutively expressed, independent of cell density. In contrast, in nontransformed human astrocytes, nuclear FGFR1 levels fluctuate with the proliferative state of the cell. In quiescent, confluent astrocytes nuclear FGFR1 protein was depleted. An accumulation of nuclear FGFR1 was observed following the transition to a subconfluent, proliferating state. Transfection of a pcDNA3.1-FGFR1 expression vector into glioma cells that do not express FGFR1 resulted in the nuclear accumulation of FGFR1, increased cell proliferation, and stimulated transition from the G₀/G₁ to the S-phase of the cell cycle. The increased proliferative rate was resistant to inhibition by the cell-impermeable FGF binding antagonist, ***myo-inositol*** hexakis (dihydrogen phosphate). Our results suggest that the constitutive nuclear presence of FGFR1 contributes to the increased proliferation of glioma cells while the transient nuclear accumulation of FGFR1 in normal astrocytes may play a role in the transition to a reactive state.

L9 ANSWER 29 OF 83 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1997:374457 CAPLUS

DOCUMENT NUMBER: 127:120475

TITLE: Clustering the adhesion molecules VLA-4 (CD49d/CD29) in Jurkat T cells or VCAM-1 (CD106) in endothelial (ECV 304) cells activates the phosphoinositide pathway and triggers Ca²⁺ mobilization

AUTHOR(S): Ricard, Isabelle; Payet, Marcel D.; Dupuis, Gilles

CORPORATE SOURCE: Fac. Medicine, Univ. Sherbrooke, Sherbrooke, QC, J1H 5N4, Can.

SOURCE: European Journal of Immunology (1997), 27(6), 1530-1538

CODEN: EJIMAF; ISSN: 0014-2980

PUBLISHER: Wiley-VCH

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Ligation of very late antigen (VLA)-4 (α .4. β .1 integrin) with a cross-linked anti- α .4 subunit monoclonal antibody (mAb) triggered a biphasic Ca²⁺ response in Jurkat cell populations and in peripheral human lymphocytes. Crosslinking vascular cell adhesion mol. (VCAM)-1 (the counter-receptor of VLA-4) in ECV 304 endothelial cells generated a biphasic Ca²⁺ response. ***Tumor*** necrosis factor-primed human umbilical cord vascular endothelial cells also responded to the cross-linked mAb with a biphasic Ca²⁺ profile. Ligated VLA-4 (Jurkat cells) or VCAM-1 (ECV 304) stimulated the prodn. of myo-inositol 1,4,5-trisphosphate. ECV 304 cells induced a biphasic Ca²⁺ response in Fura2-loaded Jurkat cells, whereas a transient response was obsd. when Jurkat cells were added to Fura2-loaded ECV 304 cells. The Ca²⁺ responses in these expts. involved VLA-4/VCAM-1 interactions since they were significantly reduced (.apprx. 80%) by prior treatment of the target cells with the relevant noncross-linked mAb. Close contact between the cells triggered mutual Ca²⁺ signaling as shown by spectrofluorimetric and confocal microscopy time-dependent recordings. Fibronectin and its CS-1 fragment (V25) triggered a sustained Ca²⁺ response in Jurkat cells (confocal microscopy). It was suggested that the VLA-4 and VCAM-1 adhesion mols. can transduce a signal that involves activation of the phosphoinositide pathway and the mobilization of Ca²⁺.

L9 ANSWER 30 OF 83 MEDLINE DUPLICATE 9

ACCESSION NUMBER: 97324238 MEDLINE

DOCUMENT NUMBER: 97324238 PubMed ID: 9178615

TITLE: On the role of calcium in the regulatory volume decrease (RVD) response in Ehrlich mouse ascites ***tumor*** cells.

AUTHOR: Jorgensen N K; Christensen S; Harbak H; Brown A M; Lambert I H; Hoffmann E K; Simonsen L O

CORPORATE SOURCE: Biochemical Department, The August Krogh Institute, University of Copenhagen, Universitetsparken 13, DK-2100 Copenhagen O, Denmark.

SOURCE: JOURNAL OF MEMBRANE BIOLOGY, (1997 Jun 1) 157 (3) 281-99. Journal code: 0211301. ISSN: 0022-2631.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199707

ENTRY DATE: Entered STN: 19970721

Last Updated on STN: 19970721

Entered Medline: 19970708

AB The putative role for Ca²⁺ entry and Ca²⁺ mobilization in the activation of the regulatory volume decrease (RVD) response has been assessed in Ehrlich cells. Following hypotonic exposure (50% osmolarity) there is: (i) no increase in cellular Ins(1,4,5)P₃ content, as measured in extracts from [2-3H] ***myoinositol*** -labeled cells, a finding at variance with earlier reports from our group; (ii) no evidence of Ca²⁺-signaling recorded in a suspension of fura-2-loaded cells; (iii) Ca²⁺-signaling in only about 6% of the single, fura-2-loaded cells at 1-mM Ca²⁺ (1% only at 0.1-mM Ca²⁺ and in Ca²⁺-free medium), as monitored by fluorescence-ratio imaging; (iv) no effect of removing external Ca²⁺ upon the volume-induced K⁺ loss; (v) no significant inhibition of the RVD response in cells loaded

with the Ca²⁺ chelator BAPTA when the BAPTA-loading is performed in K⁺ equilibrium medium; (vi) an inhibition of the swelling-induced K⁺ loss (about 50%) at 1-mM Ba²⁺, but almost no effect of charybdotoxin (100 nM) or of clotrimazole (10 microM), reported inhibitors of the K⁺ loss induced by Ca²⁺-mobilizing agonists. Thus, Ca²⁺-signaling by Ca²⁺ release or Ca²⁺ entry appears to play no role in the activation mechanism for the RVD response in Ehrlich cells.

L9 ANSWER 31 OF 83 MEDLINE

ACCESSION NUMBER: 97330867 MEDLINE

DOCUMENT NUMBER: 97330867 PubMed ID: 9187302

TITLE: HDL3-signalling in HepG2 cells involves glycosyl-phosphatidylinositol-anchored proteins.

AUTHOR: Nazih-Sanderson F; Pinchon G; Nion S; Fruchart J C; Delbart C

CORPORATE SOURCE: Unite INSERM 325, Institut Pasteur, Lille, France.

SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA, (1997 May 17) 1346 (1) 45-60.

Journal code: 0217513. ISSN: 0006-3002.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199707

ENTRY DATE: Entered STN: 19970716

Last Updated on STN: 19970716

Entered Medline: 19970701

AB In [³H]phosphatidylcholine (PC) prelabelled HepG2 cells, HDL3 stimulates a biphasic increase in 1,2-diacylglycerol (DAG). The early phase is mediated in part by a phospholipase C which is inhibited by 10 microM D 609, RHC-80267 or U-73122 and less by 100 microM propranolol. A phospholipase D is more likely involved in the late phase, as the DAG peak lags behind phosphatidic acid rise and is blocked by 100 microM propranolol. Cellular preincubation with 200 microg/ml antibodies against the ***inositolphosphoglycan*** (IPG) moiety of the GPI-anchor (Ab(IPG)), or depletion in GPI-anchored proteins by cellular pretreatment with 0.5 U/ml PI-PLC, 1 mM insulin and 2 HU/ml streptolysin-O, or depletion in membrane cholesterol content by filipin (5 microg/ml), digitonin (5 microg/ml) and cholesterol oxidase (0.5 U/ml) decreases the HDL3-signal, suggesting the involvement of a lipolytic cleavage of GPI-anchored proteins. Inhibition of proteases by 1 mM leupeptin/PMSF improves the response time to HDL3, with a DAG peak at 2-3 min. In the presence of protease-inhibitors, HDL3 releases in the culture medium several proteins with a residual IPG that binds Ab(IPG) after SDS-PAGE analysis and immunoblotting. HDL3-signalling pathways comprise tyrosine kinases, as preincubation with 100 microg/ml genistein or tyrphostin inhibits the HDL3-signal. HDL3 activates PC hydrolysis through a multistep pathway involving the cleavage of GPI-anchored proteins.

L9 ANSWER 32 OF 83 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1996:717493 CAPLUS

DOCUMENT NUMBER: 126:635

TITLE: Chemopreventive effects of myo-inositol and dexamethasone on benzo[a]pyrene and 4-(methylnitrosoamino)-1-(3-pyridyl)-1-butanone-induced pulmonary carcinogenesis in female A/J mice

AUTHOR(S): Wattenberg, Lee W.; Estensen, Richard D.

CORPORATE SOURCE: Department Laboratory Medicine Pathology, University Minnesota, Minneapolis, MN, 55455, USA

SOURCE: Cancer Research (1996), 56(22), 5132-5135

CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The objective of the present investigation was to prevent ***cancer*** of the lung by use of chemopreventive agents. Administrations of diets contg. added myo-inositol or dexamethasone singly or in combination (the

latter being the most potent) are being studied for this purpose. In previous work, the two compds. were shown to inhibit benzo(a)pyrene [B(a)P] induced pulmonary adenoma formation in female A/J mice when fed during the post-initiation period [i.e., starting 1 wk after the last of three administrations of B(a)P by oral intubation]. In the present investigation, a long readministration schedule was used, which encompasses both the initiation and the post-initiation stages of carcinogenesis. The feeding of the test compds. was started 2 wk prior to the first dose of carcinogen and continued for the duration of the expt. Under these conditions, redns. in ***tumor*** formation were: myo-inositol, 64%; dexamethasone, 56%; and both together, 86%. Addn. of both compds. resulted in the largest inhibition that has been achieved with this exptl. model as used in these investigations. Studies have begun of inhibition of 4-(methylnitrosoamino)-1-(3-pyridyl)-1-butanone-induced pulmonary adenoma formation by myo-inositol and dexamethasone. The two compds. inhibit pulmonary carcinogenesis when fed singly or in combination. When fed throughout the entire protocol, redns. in ***tumor*** formation were: myo-inositol, 46%; dexamethasone, 41%; and both together, 71% (for all three). The results of these investigations demonstrate that myo-inositol and dexamethasone inhibit pulmonary adenoma formation resulting from exposures to two major pulmonary carcinogens, B(a)P and 4-(methylnitrosoamino)-1-(3-pyridyl)-1-butanone.

L9 ANSWER 33 OF 83 MEDLINE DUPLICATE 10
 ACCESSION NUMBER: 96333396 MEDLINE
 DOCUMENT NUMBER: 96333396 PubMed ID: 8757890
 TITLE: Structural similarities among malaria toxins insulin second messengers, and bacterial endotoxin.
 AUTHOR: Caro H N; Sheikh N A; Taverne J; Playfair J H; Rademacher T W
 CORPORATE SOURCE: Molecular Medicine Unit, Department of Molecular Pathology, University College London Medical School, United Kingdom.
 SOURCE: INFECTION AND IMMUNITY, (1996 Aug) 64 (8) 3438-41.
 Journal code: 0246127. ISSN: 0019-9567.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199609
 ENTRY DATE: Entered STN: 19961008
 Last Updated on STN: 19970203
 Entered Medline: 19960926

AB Malaria toxin causes hypoglycemia and induction of ***tumor*** necrosis factor. Extracts of parasitized erythrocytes which were coeluted and copurified with one of the two subtypes of mammalian insulin-mimetic inositolphosphoglycans similarly induced fibroblast proliferation in the absence of serum. In addition, induction of ***tumor*** necrosis factor in macrophages by malaria toxin and by lipopolysaccharide from Escherichia coli was enhanced by pretreatment of these toxins with alpha-galactosidase. Thus, parasitized erythrocytes contain both soluble ***inositolphosphoglycan***-like insulin second messengers and endotoxin-like lipidic molecules.

L9 ANSWER 34 OF 83 MEDLINE DUPLICATE 11
 ACCESSION NUMBER: 96397471 MEDLINE
 DOCUMENT NUMBER: 96397471 PubMed ID: 8804365
 TITLE: Vascular endothelial growth factor stimulates protein kinase C-dependent phospholipase D activity in endothelial cells.
 AUTHOR: Seymour L W; Shoaibi M A; Martin A; Ahmed A; Elvin P; Kerr D J; Wakelam M J
 CORPORATE SOURCE: CRC Institute for Cancer Studies, University of Birmingham School of Medicine, United Kingdom.
 SOURCE: LABORATORY INVESTIGATION, (1996 Sep) 75 (3) 427-37.
 Journal code: 0376617. ISSN: 0023-6837.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199611
 ENTRY DATE: Entered STN: 19961219
 Last Updated on STN: 19961219
 Entered Medline: 19961121

AB Many tumors produce vascular endothelial growth factor (VEGF), a paracrine factor acting selectively on endothelial cells. VEGF has many effects on cultured endothelial cells and mediates angiogenesis and enhanced vascular permeability in vivo. The endothelial signal transduction pathways of VEGF represent novel targets for ***cancer*** therapy because they are readily accessible to systemically administered drugs. We have examined VEGF-stimulated signals generated in HUVEC to identify potential targets for therapeutic intervention. The transphosphatidylation reaction has been used to monitor phospholipase D (PLD) activity; total inositol phosphates have been measured after prelabeling of cells with [3H] ***myoinositol***; and intracellular free calcium has been measured using Fura-2 fluorescence. After HUVEC-stimulation with VEGF, there is an early influx of calcium (maximal by 100 seconds) followed by activation of PLD (half maximal by 100 seconds, EC50 70 pm). The PLD activity was inhibited by reducing extracellular calcium (150 nM, 50% inhibition), exposure to 12-O-tetradecanoylphorbol 13 acetate (200 nM, 24 hours, 100% inhibition), Roche 31,8220 (10 microM, 15 minutes, 72% inhibition), or genestein (100 microM, 30 minutes, 56% inhibition), which suggests a dependence on both protein kinase C and tyrosine phosphorylation. Activation of phospholipase C-catalyzed hydrolysis of phosphatidylinositol-4,5-bisphosphate was inferred from the production of inositol phosphates, although this response was slower (half maximal by 3 minutes). The phospholipase C activity was also dependent on influx of calcium and was partially inhibited by low (150 nM) extracellular calcium. PLD may be involved in mediating a number of endothelial responses to ***tumor***-secreted VEGF, notably cytoskeleton-dependent effects such as the cell migration involved in angiogenesis. This signal transduction pathway could represent an accessible and vulnerable target for ***cancer*** therapeutic intervention and has the novelty of being located within normal cells rather than ***tumor*** cells.

L9 ANSWER 35 OF 83 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 12

ACCESSION NUMBER: 96350978 EMBASE

DOCUMENT NUMBER: 1996350978

TITLE: The role of hyperglycemia and hyperinsulinemia in the pathogenesis of diabetic angiopathy.

AUTHOR: Haller H.; Drab M.; Luft F.C.

CORPORATE SOURCE: Franz Volhard Clinic, Wiltberg Strasse 50,D-13125 Berlin, Germany

SOURCE: Clinical Nephrology, (1996) 46/4 (246-255).

ISSN: 0301-0430 CODEN: CLNHBI

COUNTRY: Germany

DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 003 Endocrinology

005 General Pathology and Pathological Anatomy

028 Urology and Nephrology

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The small and large vessel disease associated with diabetes mellitus is responsible for its morbidity and mortality. Although much of the pathogenesis remains to be clarified, the role of hyperinsulinemia and hyperglycemia per se in the progression of vascular disease is beginning to emerge. Hyperinsulinemia increases the release of very low density lipoprotein (VLDL) and may also be responsible for the low HDL cholesterol levels in patients with diabetes. Hyperinsulinemia also contributes to increased blood pressure, which independently promotes vascular disease. High glucose concentrations have direct influence on intracellular signal transduction, including effects on sorbitol pathway and associated changes of pyridine nucleotides, the de novo synthesis of diacylglycerol with subsequent stimulation of protein kinase C, and possibly changes in the cellular generation of ***myoinositol***. Hyperglycemia also exerts

long-lasting changes in cellular function, which result from non-enzymatic glycosylation of matrix and membrane proteins with subsequent binding of these proteins to specific receptors. These receptors are termed the advanced glycosylation end-products (AGE) receptors. Their activation leads to an increased release of cytokines and growth factors including PDGF interleukins, TNF-.alpha., and TGF-.beta., all of which may act concomitantly in the disease process.

L9 ANSWER 36 OF 83 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. DUPLICATE 13

ACCESSION NUMBER: 97029291 EMBASE

DOCUMENT NUMBER: 1997029291

TITLE: Neurobiochemical changes from Taxol/Neupogen chemotherapy for metastatic breast carcinoma corresponds with suicidal depression.

AUTHOR: Cousins J.P.; Harper G.

CORPORATE SOURCE: J.P. Cousins, Department of Radiology, Albany Medical College, 47 New Scotland Avenue, Albany, NY 12208, United States

SOURCE: Cancer Letters, (1996) 110/1-2 (163-167).

Refs: 11

ISSN: 0304-3835 CODEN: CALEDQ

PUBLISHER IDENT.: S 0304-3835(96)04486-2

COUNTRY: Ireland

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 005 General Pathology and Pathological Anatomy

008 Neurology and Neurosurgery

016 Cancer

029 Clinical Biochemistry

030 Pharmacology

037 Drug Literature Index

038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

AB A patient under Taxol and granulocyte colony stimulating factor (G-CSF, Neupogen) treatment for metastatic breast carcinoma of the liver experienced repeated suicidal depression on days 10 and 11 of therapy. MRI and MRS were performed during the fifth and sixth cycles of chemotherapy on days 1 and 10. The MRI was normal in all four examinations. The MRS showed normal levels of metabolites on days 1 of therapy, with remarkable reproducible declines in neurobiochemicals ***myoinositol*** (23-27%), choline (20-24%), creatine (10-14%) and glutamate/glutamine (22-39%) on day 10 of therapy. The neurobiochemical declines coincided with the patient's experience of suicidal depression. Patients reporting depression during standard ***cancer*** therapy may be experiencing previously undocumented chemotherapeutic neurobiochemical imbalances or neurotoxicity.

L9 ANSWER 37 OF 83 MEDLINE DUPLICATE 14

ACCESSION NUMBER: 96414449 MEDLINE

DOCUMENT NUMBER: 96414449 PubMed ID: 8817470

TITLE: Atrial natriuretic peptide inhibits the phosphoinositide hydrolysis in murine Leydig ***tumor*** cells.

AUTHOR: Khurana M L; Pandey K N

CORPORATE SOURCE: Department of Biochemistry & Molecular Biology, Medical College of Georgia, School of Medicine, Augusta 30912, USA.

CONTRACT NUMBER: HD 25527 (NICHD)

SOURCE: MOLECULAR AND CELLULAR BIOCHEMISTRY, (1996 May 24) 158 (2) 97-105.

Journal code: 0364456. ISSN: 0300-8177.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199705

ENTRY DATE: Entered STN: 19970507

Last Updated on STN: 19970507

Entered Medline: 19970501

AB The ability of ANP to inhibit the hydrolysis of phosphoinositides was examined in [3H] ***myoinositol*** -labeled intact murine Leydig ***tumor*** (MA-10) cells. Arginine vasopressin (AVP) stimulated the formation of inositol monophosphate (IP1), inositol bisphosphate (IP2), and inositol trisphosphate (IP3) both in a time- and dose-dependent manner in MA-10 cells. ANP inhibited the AVP-induced formation of IP1, IP2, and IP3 in these cells. The inhibitory effect of ANP on the AVP-stimulated formation of IP1, IP2, and IP3 accounted for 30%, 38% and 42%, respectively, which was observed at the varying concentrations of AVP. ANP caused a dose-dependent attenuation in AVP-stimulated production of IP1, IP2 and IP3 with maximum inhibition at 100 nM concentration of ANP. The production of inositol phosphates was inhibited in the presence of 8-bromo cGMP in a dose-dependent manner, whereas dibutyryl-cAMP had no effect on the generation of these metabolites. The LY 83583, an inhibitor of guanylyl cyclase and cGMP production, abolished the inhibitory effect of ANP on the AVP-stimulated production of inositol phosphates. Furthermore, 10 microM LY 83583 also inhibited the ANP-stimulated guanylyl cyclase activity and the intracellular accumulation of cGMP by more than 65-70%. The inhibition of cGMP-dependent protein kinase by H-8, significantly restored the levels of AVP-stimulated inositol phosphates in the presence of either ANP or exogenous 8-bromo cGMP. The results of this study suggest that ANP exerts an inhibitory effect on the production of inositol phosphates in murine Leydig ***tumor*** (MA-10) cells by mechanisms involving cGMP and cGMP-dependent protein kinase.

L9 ANSWER 38 OF 83 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1996:160920 BIOSIS

DOCUMENT NUMBER: PREV199698733055

TITLE: Synthesis and iron binding studies of myo-inositol

1,2,3-trisphosphate and (racemic)-myo-inositol

1,2-bisphosphate, and iron binding studies of all

myo-inositol tetrakisphosphates.

AUTHOR(S): Spiers, Ian D.; Barker, Christopher J.; Chung, Sung-Kee;

Chang, Young-Tae; Freeman, Sally (1); Gardiner, John M.;

Hirst, Peter H.; Lambert, Peter A.; Michell, Robert H.;

Poyner, David R.; Schwalbe, Carl H.; Smith, Anthony W.;

Solomons, Kevin R. H.

CORPORATE SOURCE: (1) Dep. Pharm. Biol. Sci., Aston Univ., Aston Triangle, Birmingham B4 7ET UK

SOURCE: Carbohydrate Research, (1996) Vol. 282, No. 1, pp. 81-99.

ISSN: 0008-6215.

DOCUMENT TYPE: Article

LANGUAGE: English

AB The first syntheses of the natural products myo-inositol

1,2,3-trisphosphate and (+)- ***myoinositol*** 1,2-bisphosphate are

described. The protected key intermediates 4,5,6-tri-O-benzoyl-

myoinositol and (+)-3,4,5,6-tetra-O-benzyl-myoinositol were

phosphorylated with dibenzyl N,N-diisopropylphosphoramidite in the

presence of 1 H-tetrazole and subsequent oxidation of the phosphite. The

crystal structures of the synthetic intermediates (+)-1-O-(tert-

butyldiphenylsilyl)2,3-O-cyclohexylidene-myoinositol and

(+)-4,5,6-tri-O-benzoyl-1-O-(tert-butylidiphenylsilyl)-2,3-O-

cyclohexylidene-myoinositol are reported. myo-Inositol

1,2,3-trisphosphate, (+)- ***myoinositol*** 1,2-bisphosphate, and all

isomeric myo-inositol tetrakisphosphates were evaluated for their ability

to alter HO₂ production in the iron-catalysed Haber-Weiss reaction. The

results demonstrated that a 1,2,3-grouping of phosphates in myo-inositol

was necessary for inhibition, also that (+)-myoinositol 1,2-bisphosphate

potentiated HO₂ production. myo-Inositol 1,2,3-trisphosphate resembled

myo-inositol hexakisphosphate (phytic acid) in its ability to act as a

siderophore by promoting iron-uptake into *Pseudomonas aeruginosa*.

L9 ANSWER 39 OF 83 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1995:836482 CAPLUS

DOCUMENT NUMBER: 123:250196

TITLE: Rapid incorporation of carbon-11-labeled

diacylglycerol as a probe of signal transduction in

glioma

AUTHOR(S): Imahori, Yoshio; Ohmori, Yoshio; Fujii, Ryou;
Matsumoto, Keigo; Ueda, Satoshi
CORPORATE SOURCE: Dep. Neurosurgery, Kyoto Prefectural Univ. Medicine,
Kyoto, 602, Japan
SOURCE: Cancer Research (1995), 55(19), 4225-9
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have synthesized and characterized a positron-emitting carbon-11-labeled 1,2-diacylglycerol to study phosphoinositide turnover in ***tumor*** cells. Rapid incorporation of the 1,2-diacylglycerol was obsd. in the C6 glioma cell line. The incorporated lipid fraction consisted chiefly of phosphoinositide pool and another phospholipid pool in the proliferative state. When the state was inhibited by (-)-3D-3-deoxy-3-fluoro- ***myoinositol***, incorporation into the phosphoinositide pool decreased selectively. This suggested that phosphoinositide turnover is the leading regulator of ***tumor*** proliferation potential. On the basis of the concept of carbon-11-labeled 1,2-diacylglycerol as a specific probe for visualizing the ***tumor*** signal transduction in vivo, we obtained proliferating images of implanted C6 glioma cells in the rat brain by autoradiog. and visualized the proliferation signal in human glioma by positron emission tomog.

L9 ANSWER 40 OF 83 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1995:750368 CAPLUS
DOCUMENT NUMBER: 123:187904
TITLE: Chalones, myo-inositol and other novel inhibitors of
pulmonary carcinogenesis
AUTHOR(S): Wattenberg, Lee
CORPORATE SOURCE: Department Laboratory Medicine, Pathology, University
Minnesota, Minneapolis, MN, 55455, USA
SOURCE: Journal of Cellular Biochemistry (1995), (Suppl. 22),
162-8
CODEN: JCEBD5; ISSN: 0730-2312
PUBLISHER: Wiley-Liss
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The objective of the studies reported here has been to find novel chemopreventive agents effective against carcinogenesis of the lung. In particular, identification of suppressing agents, i.e., compds. preventing the evolution of the neoplastic process, has been sought. For this purpose, inhibition of pulmonary neoplasia in female A/J mice given the test agent starting one week after the last administration of three doses of benzo[a]pyrene has been employed as the exptl. model. Under these conditions, chalcone, 4'-methoxychalcone, myo-inositol, dexamethasone, and "terpeneless" orange oil added to the diet suppressed pulmonary adenoma formation. Chalcone and 4'-methoxychalcone are open chain flavonoids, neither of these compds. occurs naturally, and their mechanism of action is not known. Myo-Inositol is a naturally occurring compd. of particular interest because of its exceedingly low toxicity. Dexamethasone is a potent glucocorticoid. Amongst its biol. properties is the capacity to induce maturation of Type 2 alveolar cells and to stimulate prodn. of surfactant by these cells. "Terpeneless" orange oil is a fraction of orange oil consisting predominantly of compds. with carbonyl or hydroxyl groups. The constituent or constituents responsible for the inhibitory effects obsd. is not known. The above studies are in an early phase of development and their ramifications remain to be detd.

L9 ANSWER 41 OF 83 MEDLINE

ACCESSION NUMBER: 94189683 MEDLINE
DOCUMENT NUMBER: 94189683 PubMed ID: 8141254
TITLE: Calcium-dependent release of arachidonic acid in response
to purinergic receptor activation in airway epithelium.
AUTHOR: Lazarowski E R; Boucher R C; Harden T K
CORPORATE SOURCE: Department of Medicine, University of North Carolina,

Chapel Hill 27599.

CONTRACT NUMBER: GM-38213 (NIGMS)

HL-32322 (NHLBI)

SOURCE: AMERICAN JOURNAL OF PHYSIOLOGY, (1994 Feb) 266 (2 Pt 1)
C406-15.

Journal code: 0370511. ISSN: 0002-9513.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199404

ENTRY DATE: Entered STN: 19940509

Last Updated on STN: 19970203

Entered Medline: 19940428

AB The effect of purinergic receptor agonists on arachidonic acid release was investigated in [3H]arachidonic acid-prelabeled human airway epithelial cells. Exposure of bronchial epithelial BEAS39 cells to extracellular ATP resulted in a marked release of unesterified [3H]arachidonic acid with maximal effect observed within 60-90 s. [3H]diacylglycerol and [3H]phosphatidic acid accumulated in parallel with [3H]arachidonic acid. ATP-stimulated [3H]arachidonic acid release with a $K_{0.5}$ of 9 ± 2 μ M and UTP was equipotent; no effect was observed with P2Y- or P2X-purinergic receptor agonists or with adenosine. Similar results were obtained with primary cultures of normal human nasal epithelium, CF/T43 and HBE1 airway epithelial cell lines derived from a cystic fibrosis patient and from a normal donor, respectively, and HT-29 human colon carcinoma cells. ATP stimulated inositol phosphate formation in BEAS39 cells with a concentration dependence identical to that for [3H]arachidonic acid release. The effect of ATP on both [3H]arachidonic acid release and inositol phosphate formation was equally inhibited by pertussis toxin. The Ca^{2+} ionophore A-23187 mimicked the effects of ATP or UTP on arachidonic acid release, and a marked inhibitory effect was observed with thapsigargin. The protein kinase C inhibitor staurosporine partially inhibited ATP-stimulated [3H]arachidonic acid release. These data are consistent with the hypothesis that phospholipase A2 activation is secondary to P2U-purinergic receptor stimulation of D- ***myoinositol*** 1,4,5-trisphosphate production and calcium mobilization from intracellular stores.

L9 ANSWER 42 OF 83 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1994:129455 BIOSIS

DOCUMENT NUMBER: PREV199497142455

TITLE: Reduced Na^+/K^+ ATPase transport activity, resting membrane potential, and bradykinin-stimulated phosphatidylinositol synthesis by polyol accumulation in cultured neuroblastoma cells.

AUTHOR(S): Yorek, M. A. (1); Dunlap, J. A.; Stefani, M. R.; Davidson, E. P.

CORPORATE SOURCE: (1) 3E17, Veterans Affairs Med. Center, Iowa City, IA 52246 USA

SOURCE: Neurochemical Research, (1994) Vol. 19, No. 3, pp. 321-329.

ISSN: 0364-3190.

DOCUMENT TYPE: Article

LANGUAGE: English

AB In these studies we examined the effect of polyol accumulation on neural cell myo-inositol metabolism and properties. Neuroblastoma cells were cultured for two weeks in media containing 30 mM glucose, fructose, galactose or mannose with or without 0.4 mM sorbinil or 250 μ M ***myoinositol***. Chronic exposure of neuroblastoma cells to media containing 30 mM glucose, galactose, or mannose caused a decrease in myo-inositol content and myo-(2-3H)inositol accumulation and incorporation into phosphoinositides compared to cells cultured in unsupplemented medium or medium containing 30 mM fructose as an osmotic control. These monosaccharides each caused an increase in intracellular polyol levels with galactitol \approx sorbitol \approx mannitol accumulation. Chronic exposure of neuroblastoma cells to media containing 30 mM glucose, galactose, or mannose caused a significant decrease in Na^+/K^+ ATPase transport activity,

resting membrane potential, and bradykinin-stimulated ^{32}P incorporation into phosphatidylinositol compared to cells cultured in medium containing 30 mM fructose. In contrast, basal incorporation of ^{32}P into phosphatidylinositol or basal and bradykinin-stimulated ^{32}P incorporation into phosphatidylinositol 4,5-bisphosphate were not effected. Each of these cellular functions as well as myo-inositol metabolism and content and polyol levels remained near control values when 0.4 mM sorbinil, an aldose reductase inhibitor, was added to the glucose, galactose, or mannose supplemented media. ***myo-inositol*** metabolism and content and bradykinin-stimulated phosphatidylinositol synthesis were also maintained when media containing 30 mM glucose, galactose, or mannose was supplemented with 250 μM myo-inositol. The results suggest that polyol accumulation induces defects in neural cell myo-inositol metabolism and certain cell functions which could, if they occurred in vivo, contribute to the pathological defects observed in diabetic neuropathy.

L9 ANSWER 43 OF 83 MEDLINE DUPLICATE 15
 ACCESSION NUMBER: 95055065 MEDLINE
 DOCUMENT NUMBER: 95055065 PubMed ID: 7965703
 TITLE: Dual effects of nordidemnin on WRK1 cells: inhibition of phosphoinositide metabolism and cell proliferation.
 AUTHOR: Dominice C; Dufour M N; Patino N; Manzoni O; Grazzini E; Jouin P; Guillon G
 CORPORATE SOURCE: Centre National de la Recherche Scientifique UPR 9023, Montpellier, France.
 SOURCE: JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (1994 Oct) 271 (1) 107-17.
 Journal code: 0376362. ISSN: 0022-3565.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199411
 ENTRY DATE: Entered STN: 19950110
 Last Updated on STN: 19970203
 Entered Medline: 19941125

AB Nordidemnin (NorD), a cyclodepsipeptide isolated from marine invertebrates, exhibits antiproliferative and antitumoral properties identical to didemnin B on many cell lines. On WRK1 cells, a rat mammary ***tumor*** cell line, NorD considerably reduced the vasopressin-stimulated accumulation of inositol phosphates. This effect was more pronounced on dividing cells and of weak amplitude on quiescent ones. It was observed with nanomolar concentrations of NorD and became significant after 3 hr of incubation at 37 degrees C. The maximal effect was observed after a 14-hr incubation period. In contrast, the inactive analog epinordidemnin, as well as the structurally related immunosuppressive cyclosporin A, had no significant effect on phosphoinositide metabolism. More detailed analysis demonstrated that NorD reduced the amounts of all intracellular inositol phosphate isomers, including inositol pentakisphosphate and inositol hexakisphosphate. Vasopressin-stimulated inositol (1,4,5)-trisphosphate accumulation was reduced by 80% and, as a consequence, the intracellular calcium mobilization was strongly affected. Similarly, NorD reduced both the level of inositol (1,4,5)-trisphosphate and the intracellular free calcium concentration of unstimulated cells. NorD blocked phosphoinositide metabolism by reducing the ***myo-inositol*** transporter and, by a consequence, the pool of inositol lipids. NorD also strongly inhibited WRK1 cell proliferation with the same EC_{50} as that observed for the effect on phosphoinositide metabolism. Epinordidemnin, which was unable to inhibit inositol phosphate accumulation, had no effect on cell growth. Cyclosporin A, which slightly inhibited WRK1 cell growth, did not significantly affect the calcium-phosphatidylinositol cascade. Taken together, these results suggest that NorD might interfere with WRK1 cell growth by inhibiting phosphoinositide turnover.

L9 ANSWER 44 OF 83 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
 ACCESSION NUMBER: 1995:37665 BIOSIS

DOCUMENT NUMBER: PREV199598051965

TITLE: Cellular pharmacology of D-3-azido-3-deoxy-myo-inositol, an inhibitor of phosphatidylinositol signaling having antiproliferative activity.

AUTHOR(S): Brunn, G.; Fauq, A. H.; Chow, S.; Kozikowski, A. P.; Gallegos, A.; Powis, G. (1)

CORPORATE SOURCE: (1) Arizona Cancer Cent., Univ. Arizona, 1515 N. Campbell Ave., Tucson, AZ 85724 USA

SOURCE: Cancer Chemotherapy and Pharmacology, (1994) Vol. 35, No. 1, pp. 71-79.
ISSN: 0344-5704.

DOCUMENT TYPE: Article

LANGUAGE: English

AB D-3-Azido-3-deoxy-myo-inositol (3AMI) is an inhibitor of the growth of v-sis-transformed NIH 3T3 cells but not of wild-type NIH 3T3 cells, whose effects may be mediated through the phosphatidylinositol-3'-kinase pathway. We studied some properties of the cellular pharmacology of 3AMI using high-specific-activity (3H)-3AMI. The uptake of (3H)-3AMI by wild-type NIH 3T3 and v-sis NIH 3T3 cells was similar. (3H)-3AMI was a substrate for phosphatidylinositol synthetase, with the maximal velocity (V-max) being 1.0 nmol min⁻¹ mg⁻¹ and the Michaelis constant (K-m) being 23 mM. Corresponding values obtained for (3H)-myo-inositol as a substrate were 5.5 nmol min⁻¹ mg⁻¹ and 3.2 mM. (3H)-3AMI was incorporated into the cellular inositol lipids of v-sis NIH 3T3 cells to a similar extent as that observed for (3H)- ***myoinositol*** but was not incorporated into the inositol lipids of wild-type NIH 3T3 cells. The (3H)-3AMI incorporated by the v-sis NIH 3T3 cells was present in the phosphatidylinositol and phosphatidylinositol phosphate fractions but not in bisphosphorylated phosphatidylinositol. myo-Inositol antagonized the growth-inhibitory effects of 3AMI. The v-sis NIH 3T3 cells were found to be more sensitive than the wild-type NIH 3T3 cells to growth inhibition (without 3AMI) caused by the removal of myo-inositol from the medium. The results of the study suggest that 3AMI is an antimetabolite of myo-inositol. The relative sensitivity of v-sis NIH 3T3 and some other cells to 3AMI may be a reflection of increased myo-inositol requirements for the growth of these cells as compared with wild-type NIH 3T3 cells.

L9 ANSWER 45 OF 83 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 16

ACCESSION NUMBER: 93290934 EMBASE

DOCUMENT NUMBER: 1993290934

TITLE: Studies of chemopreventive effects of myo-inositol on benzo[a]pyrene-induced neoplasia of the lung and forestomach of female A/J mice.

AUTHOR: Estensen R.D.; Wattenberg L.W.

CORPORATE SOURCE: Dept Lab Medicine and Pathology, 6-153 Jackson Hall, University of Minnesota, Minneapolis, MN 55455, United States

SOURCE: Carcinogenesis, (1993) 14/9 (1975-1977).
ISSN: 0143-3334 CODEN: CRNGDP

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
016 Cancer
037 Drug Literature Index
048 Gastroenterology

LANGUAGE: English

SUMMARY LANGUAGE: English

AB There is a continuing effort at identifying chemopreventive agents that might be useful in preventing ***cancer*** of the lung. In the present study, the effects of myo-inositol and dexamethasone on benzo[a]pyrene (B[a]P)-induced pulmonary adenoma formation in female A/J mice was investigated. A diet containing 3% myo-inositol fed beginning 1 week after B[a]P administration reduced the number of pulmonary adenomas by 40% but did not prevent forestomach tumors, which also occur in this experimental model. Under the same conditions, dexamethasone, 0.5 .mu.g/g diet, inhibited pulmonary adenoma formation by 57% and also inhibited forestomach ***tumor*** formation to a similar extent. Feeding a diet

containing both myo-inositol and dexamethasone resulted in an additive effect on the inhibition of pulmonary adenoma formation. The combination of ***myo-inositol*** plus dexamethasone produced almost identical inhibition of forestomach ***tumor*** formation to that of dexamethasone alone. The results of the present study are preliminary, but may provide a basis for future investigation into strategies for chemoprevention of pulmonary neoplasia.

L9 ANSWER 46 OF 83 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 93088303 EMBASE

DOCUMENT NUMBER: 1993088303

TITLE: Lithium enhances muscarinic receptor-stimulated
CDP-diacylglycerol formation in inositol-depleted SK-N-SH
neuroblastoma cells.

AUTHOR: Stubbs Jr. E.B.; Agranoff B.W.

CORPORATE SOURCE: Neuroscience Laboratory Building, University of Michigan,
1103 East Huron, Ann Arbor, MI 48104-1687, United States

SOURCE: Journal of Neurochemistry, (1993) 60/4 (1292-1299).

ISSN: 0022-3042 CODEN: JONRA

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 008 Neurology and Neurosurgery

030 Pharmacology

032 Psychiatry

037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The psychotherapeutic action of Li⁺ in brain has been proposed to result from the depletion of cellular inositol secondary to its block of inositol monophosphatase. This action is thought to slow phosphoinositide resynthesis, thereby attenuating stimulated phosphoinositidase-mediated signal transduction in affected cells. In the present study, the effect of Li⁺ on muscarinic receptor-stimulated formation of the immediate precursor of phosphatidylinositol, CDP-diacylglycerol (CDP-DAG), has been examined in human SK-N-SH neuroblastoma cells that have been cultured under conditions that alter the cellular content of myo-inositol. Resting neuroblastoma cells, like brain cells in vivo, were found to concentrate inositol from the culture medium, achieving an intracellular level of 60.0 ± 4 nmol/mg of protein. The addition of carbachol to [3H]cytidine-prelabeled cells elicited a four- to fivefold increase in the accumulation of labeled CDP-DAG. This stimulated formation of [3H]CDP-DAG was completely blocked by the addition of 10 μM atropine, was not dependent on the presence of Li⁺, nor was it affected by co-incubation with ***myo-inositol***. This result was in sharp contrast to findings in rat brain slices, in which carbachol-stimulated formation of [3H]CDP-DAG was potentiated approx. 10-fold by Li⁺ and substantially reduced by co-incubation with inositol. The formation of [3H]CDP-DAG in labeled SK-N-SH cells by carbachol was both concentration and time dependent. The order of efficacy of muscarinic ligands in stimulating [3H]CDP-DAG accumulation paralleled that established in these cells for inositol phosphate accumulation, i.e., carbachol > oxotremorine-M > bethanecol > arecoline > oxotremorine > pilocarpine. Extended culture of the SK-N-SH cells in an inositol-free chemically defined growth medium progressively reduced the intracellular inositol content to <5 nmol/mg of protein, a level comparable with that seen in cortical slices. In these inositol-depleted cells, Li⁺ potentiated carbachol-stimulated [3H]CDP-DAG formation, and this effect was completely reversed by co-incubation with inositol (EC50 0.2 mM). The present study thus demonstrates, in the same cultured cell line, the effects of normal and reduced intracellular inositol levels on the ability of Li⁺ to attenuate phosphoinositide resynthesis, as inferred from [3H]CDP-DAG accumulation. The results indicate that Li⁺ can lead to a slowing of stimulated phosphoinositide turnover in neuroblastoma cells, provided that the intracellular inositol content has been significantly reduced.

L9 ANSWER 47 OF 83 MEDLINE

DUPLICATE 17

ACCESSION NUMBER: 94116182 MEDLINE

DOCUMENT NUMBER: 94116182 PubMed ID: 8287569
 TITLE: Pituitary adenomas with high and low basal inositol phospholipid turnover; the stimulatory effect of kinins and an association with interleukin-6 secretion.
 AUTHOR: Jones T H; Kennedy R L; Justice S K; Price A
 CORPORATE SOURCE: University Department of Medicine, Clinical Sciences Centre, Sheffield, UK.
 SOURCE: CLINICAL ENDOCRINOLOGY, (1993 Oct) 39 (4) 433-9.
 Journal code: 0346653. ISSN: 0300-0664.
 PUB. COUNTRY: ENGLAND: United Kingdom
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199402
 ENTRY DATE: Entered STN: 19940312
 Last Updated on STN: 19970203
 Entered Medline: 19940224

AB OBJECTIVE--We examined basal inositol phospholipid turnover and the response to the kinin, kallidin, in human pituitary adenomas and determined whether or not there was an association between these parameters and interleukin (IL-6) secretion status by the tumours. DESIGN--Pituitary adenoma tissue was dispersed and cells were cultured in monolayer for 96 hours. The medium was then removed and assayed for IL-6 and anterior pituitary hormones. The cells were labelled with 3H-***myoinositol*** for 24 hours and then incubated under basal conditions with kallidin and, in some cases, with TRH and GnRH for 60 minutes. Total inositol phosphate accumulation and pituitary hormone secretion were assessed. PATIENTS--Tissue was collected from 29 consecutive patients being treated surgically for pituitary adenomas. MEASUREMENTS--Total 3H-inositol phosphates, growth hormone, prolactin, LH, FSH, TSH and immunoreactive IL-6. RESULTS--Two groups of pituitary adenomas were identified, one with high and one with low basal inositol phospholipid turnover. Kallidin stimulated inositol phosphate accumulation in seven of the 29 adenomas studied. The kallidin-responsive adenomas were associated with high basal phosphoinositide turnover. All seven kallidin-responsive adenomas secreted IL-6. The adenomas studied with high basal inositol phosphate production were also responsive to TRH and in two tumours to GnRH. Kallidin stimulated GH release in one GH-secreting adenoma but had no effect on hormone secretion from any other ***tumour***. CONCLUSION--Two groups of pituitary adenomas have been identified with high and low basal inositol phosphoinositide turnover. Phosphoinositide metabolism is readily stimulated by kallidin and TRH in adenomas with high but not low turnover. Kinin-responsive adenomas secreted IL-6 but IL-6 secretor status does not preclude that they will respond to kallidin.

L9 ANSWER 48 OF 83 MEDLINE DUPLICATE 18
 ACCESSION NUMBER: 93250122 MEDLINE
 DOCUMENT NUMBER: 93250122 PubMed ID: 8387347
 TITLE: [Melanocyte-stimulating hormone induces growth of human malignant melanoma amelanotic cells with a change in cAMP, phosphatidylinositols, and inositol phosphate concentration].
 Melanotsitstimuliruiushchii gormon ingibiruet rost amelanotichnykh kletok zlokachestvennoi melanomy cheloveka s izmeneniem kontsentratsii cAMP, fosfatidilinozitolov i fosfatov inozita.
 AUTHOR: Sukhanov V A; Voronkova I M; Shvets S V; Morozova L F
 SOURCE: BIOKHIMIJA, (1993 Feb) 58 (2) 211-23.
 Journal code: 0372667. ISSN: 0320-9725.
 PUB. COUNTRY: RUSSIA: Russian Federation
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: Russian
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199306
 ENTRY DATE: Entered STN: 19930618
 Last Updated on STN: 19970203
 Entered Medline: 19930610

AB The melanocyte-stimulating hormone (alpha-MSH) used at $10(-6)$ - $5 \times 10(-8)$ M concentrations inhibited the growth of amelanotic cells of human malignant melanoma BRO and influenced cell morphology without any effect on melanization or tyrosinase activity. Inhibition of ***tumour*** cell growth was accompanied by marked elevation of intracellular cAMP levels but not that of cGMP. Dibutyl-cAMP and the cAMP-dependent protein kinase A inhibitor also inhibited the cell growth. alpha-MSH increased mono-, di- and 1,4,5- ***myoinositol*** triphosphate concentrations and influenced the activities of phosphatidylinositol kinase and phosphatidylinositol-4-phosphate kinase determining phosphatidylinositol-4-phosphate kinase and phosphatidylinositol-4,5-diphosphate levels. ***Myoinositol*** phosphate concentrations changed on a second scale and levelled off by the 3rd-5th min, whereas that of cAMP increased drastically by the 30th min.

L9 ANSWER 49 OF 83 MEDLINE DUPLICATE 19

ACCESSION NUMBER: 93275786 MEDLINE

DOCUMENT NUMBER: 93275786 PubMed ID: 8502588

TITLE: Alteration of membrane fatty acid composition and inositol phosphate metabolism in HT-29 human colon ***cancer*** cells.

AUTHOR: Awad A B; Fink C S; Horvath P J

CORPORATE SOURCE: Nutrition Program, University at Buffalo, NY 14214.

SOURCE: NUTRITION AND CANCER, (1993) 19 (2) 181-90.

Journal code: 7905040. ISSN: 0163-5581.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199306

ENTRY DATE: Entered STN: 19930716

Last Updated on STN: 19970203

Entered Medline: 19930629

AB The present study was designed to investigate the role of membrane fatty acid (FA) composition on inositol phosphate (InsP) release by a human colon ***tumor*** cell line. Cells were supplemented for five days in culture with 0, 10, 30, or 100 microM sodium stearate (18:0), linoleate [18:2(omega-6)], or linoleate [18:3(omega-3)]. These FAs were supplied as a complex with FA-free bovine serum albumin. InsP release was examined in these cells with or without stimulation with deoxycholic acid (DCA) after they were labeled with [3H] ***myoinositol***. FA enrichment was found to influence inositol incorporation into membrane lipids. Although 18:0 had no effect, 18:2(omega-6) decreased the incorporation. On the other hand, 18:3(omega-3) increased the incorporation of inositol compared with the cells supplemented with the other FAs, but they were not different from control. Basal release of total InsP was elevated only with supplementation of 10 and 30 microM 18:3(omega-3). FA supplementation with 18:0 at 30 microM and 18:2 at 30 and 100 microM resulted in downregulation of basal release of InsP. Enrichment of HT-29 cell membranes with polyunsaturated FAs resulted in a significant increase in stimulated release of InsP, but this was not seen with saturated FA supplementation. At 10 microM supplementation, 18:2 had the greatest effect on stimulated InsP release. This effect of 18:2 disappeared at 30 microM. However, the increase in the stimulated InsP release caused by 18:3 occurred at 10 and 30 microM. DCA-stimulated release of InsP was not downregulated by any FA supplementation. This study showed that enrichment of the membranes with polyunsaturated FAs increases the response of the phosphatidylinositol cycle to DCA stimulation. In addition, enrichment with 18:3(omega-3) increases the basal turnover of InsP. It is concluded that alteration of membrane FAs has a profound effect on the phosphatidylinositol cycle.

L9 ANSWER 50 OF 83 MEDLINE

ACCESSION NUMBER: 93285324 MEDLINE

DOCUMENT NUMBER: 93285324 PubMed ID: 8389720

TITLE: A product of phosphatidylinositol-3 kinase is elevated in dividing HT29 colonic epithelial cells.

AUTHOR: Dobos G J; Wu X R; Traynor-Kaplan A

CORPORATE SOURCE: Department of Medicine, University of California, San Diego

92103-8414.

CONTRACT NUMBER: 2R01DK28305 (NIDDK)
 SOURCE: FEBS LETTERS, (1993 Jun 14) 324 (2) 143-6.
 Journal code: 0155157. ISSN: 0014-5793.
 PUB. COUNTRY: Netherlands
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199307
 ENTRY DATE: Entered STN: 19930723
 Last Updated on STN: 19980206
 Entered Medline: 19930709

AB Phosphatidylinositol 3 kinase (PI-3 kinase) activity has been linked to cell proliferation and growth regulation. Therefore, we studied changes in phosphoinositide metabolism during the cell cycle of HT-29 cells, a colonic epithelial cell line. HT29 cells were treated with the microtubule disrupter, nocodazole, separated into mitotic and quiescent populations and their phospholipid composition was analyzed. Radiolabelled phospholipids from cells labelled with $^{32}\text{PO}_4$ or $[^3\text{H}]$ ***myoinositol*** were analyzed by TLC and/or deacylated and analyzed by HPLC. In all cases, levels of phosphatidylinositol 3 phosphate from mitotic phase cells were double that in resting populations. Therefore, levels of a product of PI-3 kinase are elevated and may play a role in cell division.

L9 ANSWER 51 OF 83 MEDLINE

ACCESSION NUMBER: 93302743 MEDLINE
 DOCUMENT NUMBER: 93302743 PubMed ID: 8391123
 TITLE: Aluminium impacts elements of the phosphoinositide signalling pathway in neuroblastoma cells.
 AUTHOR: Shi B; Chou K; Haug A
 CORPORATE SOURCE: Department of Microbiology, Michigan State University, East Lansing 48824.
 SOURCE: MOLECULAR AND CELLULAR BIOCHEMISTRY, (1993 Apr 21) 121 (2) 109-18.
 Journal code: 0364456. ISSN: 0300-8177.
 PUB. COUNTRY: Netherlands
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199307
 ENTRY DATE: Entered STN: 19930813
 Last Updated on STN: 20000303
 Entered Medline: 19930723

AB Inositol phosphate formation was examined in aluminium-treated murine neuroblastoma cells labelled with $[^3\text{H}]$ - ***myoinositol***. Employing fluoride-stimulated intact cells, aluminium (0.2 microM to 1 mM) reduced inositol phosphate formation in a dose-dependent manner. In digitonin-permeabilized cells, stimulated with nonhydrolyzable GTP[S], inositol phosphate formation was also inhibited by increasing aluminium doses; the IC_{50} value was about 20 microM aluminium, while the inositol phosphate level was reduced 2.5 to 3 fold by 50 microM aluminium. The inhibitory effect of aluminium (50 microM) could not be reversed by increasing GTP[S] concentrations up to 500 microM. Prechelation of aluminium to citrate or EGTA completely abolished the aluminium-triggered inhibition of fluoride-stimulated inositol phosphate formation in intact cells, but had little effect on the inhibition of permeabilized cells stimulated with GTP[S]. In neuroblastoma cells phosphoinositide hydrolysis could be evoked either through a pathway involving the Mg^{2+} /guanine nucleotide binding (Gp) protein, or via a pathway operative in the presence of high intracellular Ca^{2+} concentrations. In the Mg^{2+} /Gp protein-mediated pathway, formation of inositol triphosphate, IP_3 , inositol diphosphate, IP_2 , and inositol monophosphate, IP , was apparently inhibited by aluminium in an interdependent manner. As to the Ca^{2+} -mediated pathway, aluminium application mainly diminished the release of IP_3 . Following interiorization, aluminium thus acts upon elements critical for phosphoinositide-associated signal transduction. An aluminium target apparently resides on the Gp protein.

Phosphatidylinositol-4,5-diphosphate-specific phospholipase C probably harbours a second aluminium target.

L9 ANSWER 52 OF 83 MEDLINE DUPLICATE 20
 ACCESSION NUMBER: 92371306 MEDLINE
 DOCUMENT NUMBER: 92371306 PubMed ID: 1324151
 TITLE: 1,25-dihydroxyvitamin D3 inhibits Na(+)-H+ exchange by stimulating membrane phosphoinositide turnover and increasing cytosolic calcium in CaCo-2 cells.
 AUTHOR: Wali R K; Baum C L; Bolt M J; Brasitus T A; Sitrin M D
 CORPORATE SOURCE: Department of Medicine, University of Chicago, Illinois 60637.
 CONTRACT NUMBER: DK-26678 (NIDDK)
 DK-39573 (NIDDK)
 DK-42086 (NIDDK)
 +
 SOURCE: ENDOCRINOLOGY, (1992 Sep) 131 (3) 1125-33.
 Journal code: 0375040. ISSN: 0013-7227.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
 ENTRY MONTH: 199209
 ENTRY DATE: Entered STN: 19921009
 Last Updated on STN: 19970203
 Entered Medline: 19920922

AB We have examined the effects of 1,25-dihydroxyvitamin D3 [1,25-(OH)2D3] on the phosphoinositol signal transduction pathway in the human colon ***cancer***-derived cell line CaCo-2 and have studied the regulation of intracellular calcium ([Ca2+]i) and pH (pHi) by this secosteroid. CaCo-2 cells were prelabeled with [3H] ***myoinositol*** and treated with 10(-8) M 1,25-(OH)2D3 or vehicle for 90 sec. 1,25-(OH)2D3 caused a decrease in labeled phosphatidylinositol-4,5-bis-phosphate and an increase in labeled inositol 1,4,5-trisphosphate. Treatment with 10(-8) M 1,25-(OH)2D3 for 90 sec also raised the cellular content of diacylglycerol. In a dose-dependent manner, 1,25-(OH)2D3 caused the translocation of protein kinase-C activity from the cytosolic to the membrane fraction, which occurred after as little as 15 sec of exposure to the secosteroid, peaked at about 1-5 min, and then returned toward baseline values. In these CaCo-2 cells, baseline [Ca2+]i was 258 +/- 2 nM (mean +/- SE), as assessed using the fluorescent dye fura-2. After exposure to 10(-8) M 1,25-(OH)2D3, [Ca2+]i rapidly increased to 392 +/- 14 nM after 100 sec, fell, and then subsequently rose to a plateau of 350 +/- 3 nM after 400 sec. In Ca(2+)-free buffer, 1,25-(OH)2D3 caused only a transient rise in [Ca2+]i, indicating that 1,25-(OH)2D3 stimulated both the release of intracellular calcium stores and calcium influx. 1,25-(OH)2D3 caused a dose-dependent decrease in pHi in CaCo-2 cells, as assessed by the fluorescent dye BCECF, which was not observed in cells suspended in Na(+)-free buffer or pretreated with amiloride, indicating that the secosteroid inhibited Na(+)-H+ exchange. No effect of 1,25-(OH)2D3 on pHi was observed in cells in a Ca(2+)-free buffer or pretreated with the phospholipase-C inhibitor U-73,122, which also blocked the rise in [Ca2+]i, or in cells pretreated with the Ca2+/calmodulin inhibitor calmidazolium. Taken together, these studies indicate that 1,25-(OH)2D3 rapidly stimulates membrane phosphoinositide breakdown in CaCo-2 cells, generating the second messengers inositol 1,4,5-trisphosphate and diacylglycerol, causing translocation of protein kinase-C to the membrane, and increasing [Ca2+]i by both releasing calcium stores and promoting calcium influx. Secondary to the rise in [Ca2+]i, Na(+)-H+ exchange is inhibited by a calcium/calmodulin-dependent pathway.

L9 ANSWER 53 OF 83 MEDLINE DUPLICATE 21
 ACCESSION NUMBER: 94155157 MEDLINE
 DOCUMENT NUMBER: 94155157 PubMed ID: 1343852
 TITLE: Effects of diabetes and insulin on phosphoinositide metabolism in R3230AC mammary tumors.
 AUTHOR: Narayanan U; Hilf R

09868968

CORPORATE SOURCE: Department of Biochemistry, University of Rochester, School
of Medicine and Dentistry, New York 14642.
CONTRACT NUMBER: CA 16660 (NCI)
SOURCE: CANCER BIOCHEMISTRY BIOPHYSICS, (1992 Nov) 13 (2) 93-101.
Journal code: 7506524. ISSN: 0305-7232.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199403
ENTRY DATE: Entered STN: 19940406
Last Updated on STN: 19970203
Entered Medline: 19940325

AB The effects of diabetes and insulin administration on certain aspects of
phosphoinositide metabolism in R3230AC mammary tumors were studied in
vivo. Three weeks after diabetes was induced by streptozotocin, [3H]
myoinositol incorporation into PI, PIP and PIP2 was increased in
R3230AC tumors, whereas the formation of [3H]IP, [3H]IP2 and [3H]IP3 was
decreased. Administration of protamine zinc insulin (3IU, twice daily, for
3 days) to diabetic rats decreased [3H] ***myoinositol*** incorporation
into phosphoinositides and inositol phosphates in these mammary tumors.
The R3230AC ***tumor*** from insulin-treated diabetic hosts had lower
levels of unmetabolized [3H]- ***myoinositol*** compared to tumors from
diabetic animals. Enzymatically-dissociated ***tumor*** cells from
insulin-treated animals displayed decreased ***myoinositol***
transport in vitro. These findings suggest that the insulin-induced
decrease in the turnover of inositol lipids in vivo in R3230AC mammary
tumors could have resulted from the decreased level of [3H]
myoinositol in these cells.

L9 ANSWER 54 OF 83 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:166280 CAPLUS
DOCUMENT NUMBER: 116:166280
TITLE: Lipid peroxide-inhibiting activity of myo-inositol and
its therapeutic use
INVENTOR(S): Yoshimura, Yoshihiro; Tomita, Chihiro
PATENT ASSIGNEE(S): Tomita, Chihiro, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 2 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 03287685	A2	19911218	JP 1990-87430	19900403
PRIORITY APPLN. INFO.:			JP 1990-87430	19900403

AB Myo-inositol promoted Fe2+ oxidn. and inhibited hydroxyl radical formation
and subsequent lipid peroxidn. in vivo. Thus, myo-inositol can be used in
treating Fe2+- and hydroxyl radical-related and lipid peroxidn.-induced
myocardial infarction, ***cancer***, etc. Myo-inositol administered
to exptl. mice inhibited lipid peroxide formation in the brain and other
organs.

L9 ANSWER 55 OF 83 MEDLINE
ACCESSION NUMBER: 91340286 MEDLINE
DOCUMENT NUMBER: 91340286 PubMed ID: 1908432
TITLE: Sequence of prolactin effects on phospholipid synthesis in
Nb2 node lymphoma cells.
AUTHOR: Rillema J A; Ofenstein J P; Thul J D
CORPORATE SOURCE: Department of Physiology, Wayne State University School of
Medicine, Detroit, Michigan.
CONTRACT NUMBER: HD 06571 (NICHD)
SOURCE: HORMONE AND METABOLIC RESEARCH, (1991 May) 23 (5) 218-25.
Journal code: 0177722. ISSN: 0018-5043.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199109

ENTRY DATE: Entered STN: 19911013

Last Updated on STN: 19980206

Entered Medline: 19910926

AB In Nb2 node rat lymphoma cells, the effects of prolactin (PRL) on the rates of incorporation of several precursors into neutral lipids, phospholipids and proteins were determined. The onset of the PRL stimulation of radiolabeled-precursor incorporation into lipids occurred between 1 and 4 hours after PRL addition to Nb2 cells; precursors employed included [¹⁴C]-acetate, [³H]-glycerol, [³²P]O₄, [³H]-choline, [³H]-ethanolamine, [³H]-serine and [³H]- ***myoinositol***. No effects were observed during the initial 60 min of culture with PRL. The effects on precursor incorporation that occur after 1 hr of PRL exposure are likely related to the stimulation of cell growth by PRL. In cells that were prelabeled with the radiolabeled precursors and subsequently incubated with PRL, PRL had no effect on the metabolism of the radiolabeled phospholipids or the accumulation of phospholipid products until several hours after hormone addition. We would conclude from these studies that the initial (60 min) effect of PRL on Nb2 node lymphoma cells does not likely use a signal transduction mechanism that involves products derived from the cellular phospholipids.

L9 ANSWER 56 OF 83 MEDLINE

ACCESSION NUMBER: 91003990 MEDLINE

DOCUMENT NUMBER: 91003990 PubMed ID: 2170005

TITLE: Suramin alters phosphoinositide synthesis and inhibits growth factor receptor binding in HT-29 cells.

AUTHOR: Kopp R; Pfeiffer A

CORPORATE SOURCE: Department of Surgery, University of Munich, West Germany.

SOURCE: CANCER RESEARCH, (1990 Oct 15) 50 (20) 6490-6.

Journal code: 2984705R. ISSN: 0008-5472.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199011

ENTRY DATE: Entered STN: 19910117

Last Updated on STN: 20000303

Entered Medline: 19901121

AB Initiation of cell growth frequently involves activation of growth factor receptor-coupled tyrosine kinases and stimulation of the phosphoinositide second messenger system. The antitrypanosomal and antifilarial drug suramin has been shown to exert antiproliferative activities by inhibition of growth factor receptor binding. We therefore investigated the effect of suramin on epidermal growth factor receptor-binding characteristics and, additionally, searched for effects on basal or cholinergically stimulated phospholipid metabolism in HT-29 cells. Suramin caused a dose-dependent and noncompetitive inhibition of 125I-epidermal growth factor binding (concentration producing 50% inhibition, 44.2 micrograms/ml) but did not alter muscarinic receptor binding. Suramin did not affect the basal ³²P incorporation into phosphoinositides at concentrations of less than 200 micrograms/ml suramin. In contrast, the carbachol-stimulated enhancement of ³²P incorporation into phosphatidic acid, phosphatidylinositol, and polyphosphoinositides was reduced by 48-95% in the presence of 100 micrograms/ml suramin. Thus, phosphoinositide and diacylglycerol kinases involved in basal and receptor-stimulated phosphoinositide metabolism may be localized in different subcellular compartments, which can be dissociated by the use of suramin. Direct measurements of phosphatidylinositol kinase and diacylglycerol kinase activities showed a potent inhibition when treated with suramin. Suramin did not affect the stimulation of phospholipase C by carbachol, determined by release of [³H]inositol phosphates in [³H] ***myoinositol*** -prelabeled cells. Our data indicate that suramin potently inhibits phosphoinositide resynthesis under stimulated conditions. Additionally, we confirm the inhibitory

09868968

effects of suramin on epidermal growth factor receptor binding in a human intestinal cell line. The inhibitory effects of suramin on phospholipid metabolism may play a role in the antiproliferative actions of this drug.

L9 ANSWER 57 OF 83 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 22

ACCESSION NUMBER: 90040635 EMBASE

DOCUMENT NUMBER: 1990040635

TITLE: Neuroparsins induce phosphoinositide breakdown in the migratory locust rectal cells.

AUTHOR: Fournier B.

CORPORATE SOURCE: Laboratoire de Neuroendocrinologie des Insectes, Universite de Bordeaux I, Avenue des Facultes, 33405 Talence Cedex, France

SOURCE: Comparative Biochemistry and Physiology - B Biochemistry and Molecular Biology, (1990) 95/1 (57-64).
ISSN: 0305-0491 CODEN: CBPBB8

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 037 Drug Literature Index

029 Clinical Biochemistry

030 Pharmacology

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Neuroparsin (Nps) antidiuretic (AD) signal transduction in migratory locust rectal cells is mediated by phosphoinositide turnover and calcium ion (Ca²⁺). Using the suitable biological in-vitro assay of everted rectum and selective stimulators of protein kinase C (PKC), 1-stearoyl-2-arachidonoyl-sn-glycerol (SAG) and active phorbol ester ***tumor*** promotor or phorbol-12-myristate-13-acetate (PMA), we provoked an increase of fluid reabsorption, while polymixin B (PKC inhibitor) abolished Nps, SAG or PMA induced AD processes. ***Myoinositol*** (MI) as well as an intracellular Ca²⁺ increase obtained with the use of both Ca²⁺ ionophores A23187 and ionomycin stimulated fluid reabsorption, as Nps do. Lithium (as lithium chloride) blocked entirely the AD effects of Nps, while it inhibited partially the AD actions of MI and SAG. The level of lithium action was discussed, and participation of an inositol triphosphate was formulated as an hypothesis. Stimulation of the phosphoinositide turnover following transduction of the Np AD signal caused a simultaneous inhibition of two other second messenger systems previously found in the migratory locust rectal cells: cyclic adenosine monophosphate (cAMP) mediating AD signal generated by a factor from the glandular lobes of the corpora cardiaca, and cyclic guanosine monophosphate (cGMP) supposed to be located in rectal muscular cells. The respective decreases of cAMP and cGMP were due probably to an activation of the cyclic nucleotide dependent phosphodiesterases by Ca²⁺. The data are consistent with an important role of PKC and Ca²⁺ in modulating the AD responses of insect rectal cells, and a scheme on possible ways followed in transduction of the AD signals was proposed as a working hypothesis.

L9 ANSWER 58 OF 83 MEDLINE DUPLICATE 23

ACCESSION NUMBER: 90160064 MEDLINE

DOCUMENT NUMBER: 90160064 PubMed ID: 2154736

TITLE: Phosphoinositide metabolism in human prostate ***cancer*** cells in vitro.

AUTHOR: Wilding G; Gelmann E P; Freter C E

CORPORATE SOURCE: University of Wisconsin Clinical Cancer Center, Madison 53792.

CONTRACT NUMBER: R29-CA50590 (NCI)

SOURCE: PROSTATE, (1990) 16 (1) 15-27.

Journal code: 8101368. ISSN: 0270-4137.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199003

ENTRY DATE: Entered STN: 19900601

Last Updated on STN: 19970203

Entered Medline: 19900329

AB To understand better the mechanism by which 5-alpha-dihydrotestosterone (5-alpha-DHT) influences prostate epithelial cell function, we examined the effects of 5-alpha-DHT on phosphoinositide metabolism in human prostate ***cancer*** cell lines. Androgen receptor-positive LN-CaP cells showed dose-responsive, steady-state elevations in phosphoinositide metabolism when treated with 5-alpha-DHT. The intracellular pool of 3H-***myoinositol*** decreased and the incorporation of 3H-***myoinositol*** into cellular lipids increased with increasing concentrations of 5-alpha-DHT. 5-alpha-DHT increased the release of 3H-inositol phosphates into the media. The inactive stereoisomer, 5-beta-DHT, did not increase phosphoinositide metabolism. In androgen receptor-negative cells, phosphoinositide metabolism was not altered by 5-alpha-DHT. The slow induction of phosphoinositide metabolism by 5-alpha-DHT suggests that the effects may be mediated through other factors that serve as intermediates in 5-alpha-DHT modulation of intracellular signalling. We conclude that this modulation involves increased turnover of phosphatidylinositol, incorporation of ***myoinositol*** into cellular lipids, and alterations in the aqueous intracellular ***myoinositol*** pool size, possibly as a result of altered transport mechanisms.

L9 ANSWER 59 OF 83 MEDLINE

ACCESSION NUMBER: 90028426 MEDLINE

DOCUMENT NUMBER: 90028426 PubMed ID: 2553131

TITLE: Metabolic changes in undifferentiated and differentiated human colon adenocarcinoma cells studied by multinuclear magnetic resonance spectroscopy.

AUTHOR: Galons J P; Fantini J; Vion-Dury J; Cozzone P J; Canioni P

CORPORATE SOURCE: Centre de Resonance Magnetique Biologique et Medicale, URA CNRS, Faculte de Medecine, Marseille, France.

SOURCE: BIOCHIMIE, (1989 Aug) 71 (8) 949-61.

Journal code: 1264604. ISSN: 0300-9084.

PUB. COUNTRY: France

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198912

ENTRY DATE: Entered STN: 19900328

Last Updated on STN: 19970203

Entered Medline: 19891212

AB Aspects of energetic and intermediary metabolism were studied in a colon adenocarcinoma cell line (HT29) by multinuclear magnetic resonance spectroscopy. Experiments were carried out on the HT29-D4 clone, which was isolated by limit dilution techniques. This clone, usually undifferentiated (D4-UD), can be maintained in a differentiated state (D4-D) in a glucose-free medium. Metabolic data were obtained by NMR analysis of perchloric acid extracts from D4-UD and D4-D cells. Phosphorus-31 and proton NMR spectra showed the presence of a large amount of choline and phosphorylcholine in the differentiated state (400% and 200%, respectively, of the levels found in D4-UD cells). Other differences appeared in the content of phosphocreatine (absent in D4-D cells) and ***myoinositol*** (absent in D4-UD cells). Carbon-13 spectra were recorded from perchloric acid extracts of cells incubated with [1-13C]-labeled glucose or [2-13C]-labeled acetate. The data indicated that both types of cells metabolize glucose through the glycolytic pathway to give lactate, but only D4-D cells were able to store glucose as glycogen at a very high level. A mathematical analysis of fluxes through the tricarboxylic acid (TCA) cycle was developed on the basis of models derived from previous 14C tracer studies. The model was based on the steady-state labeling of glutamate carbons by the 13C isotope and gave the fraction of labeled acetyl-CoA entering the TCA cycle, and the activity y of anaplerotic reactions relative to the flux through the citrate synthetase reaction. The data indicated that y greater than 0.3 in all cases. Only 15% and 30% of labeled acetyl CoA entered the TCA cycle in D4-UD and D4-D cells, respectively, under labeled glucose incubation: these values were significantly different upon labeled acetate feeding,

reaching 55% for D4-UD cells and 85% for D4-D cells. The main result of this study is that the process of differentiation of HT29 cells is correlated with a large increase in the activity of oxidative metabolism.

L9 ANSWER 60 OF 83 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1989:149614 CAPLUS

DOCUMENT NUMBER: 110:149614

TITLE: Lithium-induced teratogenesis in frog embryos
prevented by a polyphosphoinositide cycle intermediate
or a diacylglycerol analog

AUTHOR(S): Busa, William B.; Gimlich, Robert L.

CORPORATE SOURCE: Dep. Biol., Johns Hopkins Univ., Baltimore, MD, 21218,
USA

SOURCE: Developmental Biology (Orlando, FL, United States)
(1989), 132(2), 315-24
CODEN: DEBIAO; ISSN: 0012-1606

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effect of a microinjection of LiCl into prospective ventral blastomeres of the 32-cell *Xenopus laevis* embryo (which gives rise to duplication of dorsoanterior structures such as the notochord, neural tube, eyes, and cement gland) is prevented by coinjection of equimolar myo-inositol, an intermediate of the polyphosphoinositide cycle. In contrast, epi-inositol, a nonbiol. positional isomer of inositol not employed in this cycle, is ineffective at rescuing Li⁺-injected embryos. Treatment of embryos at stage 7 with the ***tumor*** promoter, phorbol myristate acetate (an analog of the polyphosphoinositide cycle-derived second messenger, diacylglycerol), also prevents dorsoanterior duplication of Li⁺ embryos, while the nontransforming analog, phorbol myristate acetate-4-O-Me ether, is without effect. Both of these rescuing agents are without obvious effects on development when administered alone (i.e., without Li⁺). Li⁺-selective microelectrode measurements demonstrate that intracellular Li⁺ levels are identical when Li⁺ is injected with or without myo-inositol. Clonal anal. shows that blastomeres injected with Li⁺ plus myo-inositol make a normal contribution of progeny to the later embryo. Because Li⁺ is an inhibitor of the polyphosphoinositide cycle and can thereby have profound effects on cellular myo-inositol and diacylglycerol levels, these observations concerning inositol-mediated rescue suggest a role for altered polyphosphoinositide cycle activity in lithium-induced teratogenesis.

L9 ANSWER 61 OF 83 MEDLINE

ACCESSION NUMBER: 89164306 MEDLINE

DOCUMENT NUMBER: 89164306 PubMed ID: 2923133

TITLE: Characterization of phospholipase C activity of the plasma
membrane and cytosol of an osteoblast-like cell line.

AUTHOR: Suzuki Y; Hruska K A; Reid I; Alvarez U M; Avioli L V

CORPORATE SOURCE: Division of Bone and Mineral Diseases, Jewish Hospital of
St. Louis, MO 63110.

CONTRACT NUMBER: AM09976 (NIADDK)
AM32087 (NIADDK)

SOURCE: AMERICAN JOURNAL OF THE MEDICAL SCIENCES, (1989 Mar) 297
(3) 135-44.
Journal code: 0370506. ISSN: 0002-9629.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 198904

ENTRY DATE: Entered STN: 19900306

Last Updated on STN: 19970203

Entered Medline: 19890412

AB The properties of phospholipase C (PL-C) in the plasma membranes (PM) and the cytosol of osteoblast-like osteosarcoma cells, UMR-106, were analyzed to see if separate enzymes or similar enzymes were involved in signalling, transduction, and arachidonate release. The cytosolic PL-C displayed substrate affinities in the order of phosphatidylinositol (PI) greater

than phosphatidylinositol-4-phosphate (PIP) or phosphatidylinositol-4, 5-bisphosphate (PIP₂). Hydrolysis of PI, PIP, and PIP₂ by cytosolic PL-C was not affected by GTP or GTP gamma S and other nucleotides. PI hydrolysis by PM and cytosolic PL-C was undetectable in the presence of 500 microM EGTA and displayed two activity plateaus at various concentrations of Ca²⁺. The K_m for Ca²⁺ in the PL-C activity of the first plateau was 0.08 microM. Significant hydrolysis of PIP₂ by cytosolic PL-C was observed in the absence of Ca²⁺. In contrast to the enzyme(s) predominant in the cytosol, the order of substrate affinities for PM PL-C was PIP₂ greater than PIP greater than PI. Only PIP₂ hydrolysis by PM PL-C was stimulated by both GTP and GTP gamma S in a dose-dependent manner. PIP₂ hydrolysis by PL-C of the PM was not observed in the absence of Ca²⁺, serving to further discriminate this enzyme activity from that of the cytosol. PIP₂ hydrolysis by PL-C of the PM also was biphasic in the dependence on Ca²⁺. At resting cytosolic Ca²⁺ levels, the V_{max} of the high affinity activity already had been achieved. Guanine nucleotide stimulation of PIP₂ hydrolysis by PM PL-C was characterized by increased maximum activity with an unchanged K_m for Ca²⁺ or for PIP₂. The pH optimum of PIP₂ hydrolysis was similar between cytosolic and PM forms of PL-C. PIP₂ hydrolysis with production of IP₃ (PL-C activity) in UMR-106 cells treated with [2-3H]- ***myoinositol*** was stimulated by PTH, and this stimulation was not inhibited by pertussis toxin. These data suggest that UMR-106 cells possess at least two distinct PL-C activities, one predominant in the cytosol and activated by increasing cytosolic Ca²⁺ with PI as the substrate. The second enzyme, a GTP-activated PIP₂-specific PL-C in the plasma membranes may play an important role in hormone-induced PIP₂ hydrolysis mediated through guanine nucleotide regulatory proteins and may participate in the hormonal regulation of osteoblast cytosolic Ca²⁺ and bone remodeling functions.

L9 ANSWER 62 OF 83 MEDLINE DUPLICATE 24
 ACCESSION NUMBER: 90198396 MEDLINE
 DOCUMENT NUMBER: 90198396 PubMed ID: 2629878
 TITLE: Effect of dimethylsulfoxide on human gliomas: correlations between the nuclear magnetic resonance spectra and the transformed phenotypes of the ***tumor*** cells.
 AUTHOR: Geder L; Metz K R; Towfighi J; Mikus J L; Williams G D; Gaydos A J; Kreider J W
 CORPORATE SOURCE: Division of Neurology, Milton S. Hershey Medical Center, Pennsylvania State University, Hershey.
 SOURCE: NEUROFIBROMATOSIS, (1989) 2 (1) 23-34.
 Journal code: 8807525. ISSN: 1010-5662.
 PUB. COUNTRY: Switzerland
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199005
 ENTRY DATE: Entered STN: 19900601
 Last Updated on STN: 19970203
 Entered Medline: 19900502

AB Prolonged in vitro induction of six established human glioma cell lines with dimethylsulfoxide (DMSO) generated an adherent human fibroblastoid phenotype. The development of contact-inhibited cell growth coincided with the decreased colony-forming potential of these cells in semisolid medium and with the reduction or elimination of tumorigenicity when transplanted in athymic nude mice. These DMSO-induced changes persisted for at least 19 passages after removal of the inducer from the medium. High-resolution natural-abundance ¹³C nuclear magnetic resonance spectroscopy showed specific spectral differences between the cell lines with more or less malignant transformed phenotypes: the glioma cells with a higher degree of tumorigenicity and colony-forming potential exhibited more intense ***myoinositol*** signals than those with the more benign phenotype.

L9 ANSWER 63 OF 83 MEDLINE DUPLICATE 25
 ACCESSION NUMBER: 88228019 MEDLINE
 DOCUMENT NUMBER: 88228019 PubMed ID: 2897365
 TITLE: An autocrine factor from Reuber hepatoma cells that

stimulates DNA synthesis and acetyl-CoA carboxylase.
Characterization of biologic activity and evidence for a
glycan structure.

AUTHOR: Witters L A; Watts T D
CORPORATE SOURCE: Department of Medicine, Dartmouth Medical School, Hanover,
New Hampshire 03756.
CONTRACT NUMBER: DK35712 (NIDDK)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1988 Jun 15) 263 (17)
8027-36.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198807
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19970203
Entered Medline: 19880713

AB Conditioned medium from Reuber H-35 or Fao hepatoma cells contains
autocrine factors that both stimulate DNA synthesis and activate
acetyl-coenzyme A (CoA) carboxylase in serum-deprived Fao cells. The
factor(s), which appears within 4 h of serum-free culture, also increases
the cell number and the mitotic index. The effects of the conditioned
medium are insulinomimetic, both with respect to stimulation of DNA
synthesis and acetyl-CoA carboxylase activity. However, no induction of
tyrosine aminotransferase activity or stimulation of aminoisobutyric acid
uptake is seen in response to the conditioned medium. Insulin over a 4-h
period does not increase the concentration of DNA synthesis stimulating
activity that is observed in the medium. This activity is dialyzable and
is resistant to acid treatment or to heating to 60-100 degrees C and to
trypsin digestion; it is not extracted with chloroform/methanol nor
adsorbed by charcoal or by a C18 reverse-phase column. Fractionation of
the conditioned medium derived from Reuber H-35 hepatoma cells by gel
filtration chromatography reveals two low molecular weight (less than
1000) compounds that both stimulate DNA synthesis in Fao hepatoma cells.
The larger compound (peak I) also stimulates the activity of acetyl-CoA
carboxylase. The stimulatory effects of the peak I compound are destroyed
by nitrous acid deamination, periodate oxidation, and methanolysis.
Biosynthetic labeling studies indicate the probable presence of
glucosamine, galactose, and perhaps phosphate in the peak I-activating
material. No significant incorporation of either ***myoinositol*** or
mannose into the active material has been observed. These data, taken
together, are consistent with a glycan structure for this autocrine
factor, which bears strong resemblance to similar insulinomimetic factors
generated in BC3H1 myocytes and H-35 hepatoma cells in response to insulin
and on digestion of membranes with a phosphatidylinositol-specific
phospholipase C. Further characterization of this factor may provide
insight into different pathways of insulin action and could provide a
strategy to check autocrine-stimulated ***tumor*** growth.

L9 ANSWER 64 OF 83 MEDLINE
ACCESSION NUMBER: 88283569 MEDLINE
DOCUMENT NUMBER: 88283569 PubMed ID: 2840272
TITLE: Regulation of phosphoinositide hydrolysis in transformed
human endometrial cells.
AUTHOR: Weiss D J; Gurside E
CORPORATE SOURCE: Department of Pharmacology, Mt. Sinai School of Medicine,
City University of New York, New York 10029.
CONTRACT NUMBER: CA-15648 (NCI)
GM-07163 (NIGMS)
SOURCE: ENDOCRINOLOGY, (1988 Aug) 123 (2) 981-90.
Journal code: 0375040. ISSN: 0013-7227.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198808

ENTRY DATE: Entered STN: 19900308
 Last Updated on STN: 19970203
 Entered Medline: 19880829

AB Addition of the cholinergic agents acetylcholine or carbamylcholine (CCh) to suspensions of human endometrial adenocarcinoma cells (Ishikawa line) preincubated with [3H] ***myoinositol*** promoted a rapid concentration-dependent hydrolysis of labeled phosphoinositides to inositol tris-, bis-, and monophosphates with EC50 values (mean +/- SE) of 3.5 +/- 1.6 and 26.5 +/- 4.8 microM, respectively. Atropine inhibition of the CCh effects (Ki = 1.6 +/- 1.3 nM) and the ineffectiveness of nicotinic antagonists indicate involvement of a muscarinic receptor. Both basal and CCh-stimulated production of inositol phosphates were higher in the presence of LiCl. The effect of LiCl on inositol monophosphate accumulation was concentration dependent (1-100 mM). Vasopressin, oxytocin, phenylephrine, histamine, and prostaglandin F2 alpha, had no apparent effect on inositol phosphate levels. Phorbol esters inhibited up to 35% of the effect of CCh on inositol phosphate accumulation. Triphenylethylene antiestrogens at micromolar concentrations increased inositol phosphate accumulation, but inhibited the effects of CCh. However, the rapid uptake of trypan blue observed after exposure to 10 microM tamoxifen suggests an alteration of the plasma membrane which may affect signal-transducing systems. The effects of CCh on the production of inositol phosphates and the expected concomitant liberation of diacylglycerol by transformed epithelial cells of human endometrium are of potential significance in normal endometrial physiology, since cholinergic innervation of endometrial glands has been reported, and the role of hormonally stimulated phosphoinositide hydrolysis in secretory mechanisms has been demonstrated in many systems.

L9 ANSWER 65 OF 83 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1988:132235 CAPLUS

DOCUMENT NUMBER: 108:132235

TITLE: Design, synthesis, and biological evaluation of
 compounds of interest in the chemotherapy of
 cancer

AUTHOR(S): Jiang, Cong

CORPORATE SOURCE: Univ. Alabama, University, AL, USA

SOURCE: (1987) 241 pp. Avail.: Univ. Microfilms Int., Order
 No. DA8720696

From: Diss. Abstr. Int. B 1987, 48(6), 1671

DOCUMENT TYPE: Dissertation

LANGUAGE: English

AB Unavailable

L9 ANSWER 66 OF 83 MEDLINE

ACCESSION NUMBER: 87144570 MEDLINE

DOCUMENT NUMBER: 87144570 PubMed ID: 3029593

TITLE: Independent phosphatidylinositol synthesis in pituitary
 plasma membrane and endoplasmic reticulum.

AUTHOR: Imai A; Gershengorn M C

SOURCE: NATURE, (1987 Feb 19-25) 325 (6106) 726-8.

Journal code: 0410462. ISSN: 0028-0836.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198704

ENTRY DATE: Entered STN: 19900303

Last Updated on STN: 19980206

Entered Medline: 19870401

AB Phosphatidylinositol (PtdIns), the most abundant phosphoinositide, is the precursor of phosphatidylinositol 4-monophosphate which is converted to phosphatidylinositol 4,5-bisphosphate, the lipid hydrolysed as an early step in signal transduction by many stimuli. It is generally thought that a single enzyme in the endoplasmic reticulum, PtdIns synthase (CDP-diglyceride: ***myoinositol*** 3-phosphatidyltransferase, EC 2.7.8.11), is responsible for PtdIns synthesis and that newly synthesized

PtdIns is transported to the plasma membrane by exchange proteins. Several investigators have proposed that there are two functionally distinct pools of PtdIns, one responsive to stimulation and the other not, and that the stimulus-responsive pool may be synthesized at a different site within the cell, perhaps within the plasma membrane. Indeed, it was suggested that there is PtdIns synthase activity in plasma membrane isolated from rat liver. GH3 rat pituitary ***tumour*** cells are an excellent model system to study stimulation of phosphoinositide metabolism by thyrotropin-releasing hormone (TRH). Conversion of PtdIns to polyphosphoinositides and TRH (and GTP)-activated phosphoinositide hydrolysis are known to occur in plasma membrane isolated from GH3 cells. Here we report that PtdIns synthase activity in the plasma membrane of GH3 cells is distinct from that present in the endoplasmic reticulum. The plasma membrane PtdIns synthase may be responsible for a portion of PtdIns re-synthesis that occurs during cell stimulation.

L9 ANSWER 67 OF 83 MEDLINE DUPLICATE 26
 ACCESSION NUMBER: 87193369 MEDLINE
 DOCUMENT NUMBER: 87193369 PubMed ID: 3570557
 TITLE: Differential expression of endogenous sugar-binding proteins (lectins) in murine ***tumor*** model systems with metastatic capacity.
 AUTHOR: Gabius H J; Bandlow G; Schirmacher V; Nagel G A; Vehmeyer K
 SOURCE: INTERNATIONAL JOURNAL OF CANCER, (1987 May 15) 39 (5) 643-8.
 Journal code: 0042124. ISSN: 0020-7136.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 198706
 ENTRY DATE: Entered STN: 19900303
 Last Updated on STN: 19900303
 Entered Medline: 19870619

AB In order to investigate possible differences in sugar binding activities of strongly versus weakly metastatic tumors, sugar-binding molecules (endogenous lectins) of murine ***tumor*** cells differing in metastatic capacity were analyzed by affinity chromatography on supports with immobilized sugars or glycoproteins and compared. After elution with specific sugar in the absence of Ca²⁺-ions, the proteins were separated by sodium dodecyl sulfate-polyacrylamide slab gel electrophoresis. In comparison to a weakly metastatic subline (Eb) spontaneous strongly metastatic variants (ESb) of a murine lymphoma contained additional sugar receptors for N-acetylglucosamine (Mr 30 kDa) and maltose (Mr 64 kDa, 62 kDa, 54 kDa and 32 kDa), and lacked one sugar receptor for ***myo-inositol*** (Mr 85 kDa), N-acetylglucosamine (Mr 23 kDa) and maltose (Mr 22 kDa), respectively. The strongly metastatic variant ESb expressed the common beta-galactoside-specific lectin to a higher extent and receptors for myo-inositol, melibiose and mannan to a lower extent. In another model system derived from the murine mastocytoma cell line P 815 X 2A, biochemical analysis of the liver-metastasizing variant P 815 X 2B revealed additional characteristic N-acetylgalactosamine- and maltose-specific binding proteins. This variant had reduced amounts of receptors for beta-galactosides and fucose in comparison to the parental clone. In a third ***tumor*** system a similar qualitative difference was disclosed: a metastatic variant derived from splenic metastases displayed a sugar receptor profile with 5 additional beta-galactoside-binding proteins when compared to its parental clone 6-6#3 + F, which is a virally transformed fibroblast line. The results show that metastatic variants of 3 murine ***tumor*** models consisting of lymphomas, mastocytomas and sarcomas are characterized by qualitative and quantitative alterations in the profiles of sugar-binding proteins.

L9 ANSWER 68 OF 83 MEDLINE DUPLICATE 27
 ACCESSION NUMBER: 87083472 MEDLINE
 DOCUMENT NUMBER: 87083472 PubMed ID: 3793728

09868968

TITLE: Observation of myo-inositol 1,2-(cyclic) phosphate in a
Morris hepatoma by ³¹P NMR.
AUTHOR: Graham R A; Meyer R A; Szwergold B S; Brown T R
CONTRACT NUMBER: CA 06927 (NCI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1987 Jan 5) 262 (1) 35-7.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198702
ENTRY DATE: Entered STN: 19900302
Last Updated on STN: 19970203
Entered Medline: 19870218

AB We have identified an unusual resonance at 16.5 ppm in the ³¹P NMR spectrum of a Morris (7777) hepatoma grown in the inguinal fossa of a Buffalo rat as ***myoinositol*** 1,2-(cyclic) phosphate. This compound has been observed in all of the 32 tumors examined as well as in cultured cells derived from the ***tumor***, but it has not been observed in normal rat tissues. Its level in the aqueous phase of chloroform/methanol/water extracts of the ***tumor*** is 70 +/- 40 nmol/g, wet weight (n = 4). The presence of a breakdown product of phosphatidylinositol at such high levels in a fast growing ***tumor*** may provide an important clue for understanding the metabolic defect that results in the malignant growth of this ***tumor***.

L9 ANSWER 69 OF 83 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1986:396300 BIOSIS

DOCUMENT NUMBER: BA82:81780

TITLE: TRH STIMULATION OF POLYPHOSPHOINOSITIDE HYDROLYSIS IN GH-3
CELL MEMBRANES IS GTP DEPENDENT BUT INSENSITIVE TO CHOLERA
OR PERTUSSIS TOXIN.

AUTHOR(S): MARTIN T F J; BAJJALIEH S M; LUCAS D O; KOWALCHYK J A

CORPORATE SOURCE: ZOOLOGY RESEARCH BUILDING, UNIV. WISCONSIN, 1117 WEST
JOHNSON ST., MADISON, WI 53706.

SOURCE: J BIOL CHEM, (1986) 261 (22), 10141-10149.

CODEN: JBCHA3. ISSN: 0021-9258.

FILE SEGMENT: BA; OLD

LANGUAGE: English

AB Thyrotropin-releasing hormone (TRH), like numerous other Ca²⁺-mobilizing agonists, has been found to stimulate polyphosphoinositide hydrolysis in responsive cells. The present studies further clarify the mechanism of action of this peptide hormone by demonstrating direct in vitro effects of TRH on polyphosphoinositide hydrolysis in GH3 pituitary cell membranes. Membranes from [³H] ***myoinositol*** -labeled cells were found to generate inositol bis- and tris- but not monophosphate upon incubation. Inositol polyphosphate generation was stimulated 2-3-fold by nanomolar concentrations of TRH in a reaction which was potentiated by micromolar concentrations of GTP; hormone-stimulated hydrolysis observed in the absence of GTP was fully antagonized by guanosine 5'-O-(2-thiodiphosphate). Guanosine 5'-O-(3-thiotriphosphate), Ca²⁺, and sodium fluoride also activated phosphoinositide hydrolysis in vitro. Stimulated inositol polyphosphate generation was accompanied by stimulated 1,2-diacylglycerol formation. Evidence that both phosphatidylinositol 4,5-bisphosphate as well as phosphatidylinositol 4-phosphate served as substrates for the activated phosphoinositide phosphodiesterase is presented. Pretreatment of GH3 cells with cholera or pertussis toxin did not influence stimulated hydrolysis in membranes. It is concluded that the TRH receptor directly regulates polyphosphoinositide hydrolysis in GH3 cell plasma membranes by a GTP-dependent process. The GTP dependence does not appear to be mediated through a cholera or pertussis toxin substrate and may involve a novel GTP-binding protein (NP).

L9 ANSWER 70 OF 83 MEDLINE DUPLICATE 28

ACCESSION NUMBER: 87063807 MEDLINE

DOCUMENT NUMBER: 87063807 PubMed ID: 3641033

TITLE: The role of oxygen deficiency and cytosolic reactions in

cell growth.

AUTHOR: Macfarlane C M
 SOURCE: MEDICAL HYPOTHESES, (1986 Oct) 21 (2) 185-92.
 Journal code: 7505668. ISSN: 0306-9877.
 PUB. COUNTRY: ENGLAND: United Kingdom
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 198701
 ENTRY DATE: Entered STN: 19900302
 Last Updated on STN: 19900302
 Entered Medline: 19870113

AB It has been suggested that a decrease in the availability of oxygen to certain tissues may lead to increased metabolism of glucose through the hexose monophosphate shunt pathway and to increased synthesis of polyols, in particular ***myoinositol***. It is further suggested that these "cytosolic reactions" result in stimulation of the phosphatidylinositol cycle by increasing substrate availability (i.e. phosphatidate, diglyceride and inositol). A relative decrease in local oxygen availability may therefore play a role in cell proliferation and differentiation and in the etiology of ***cancer***, diabetic sequelae and obesity.

L9 ANSWER 71 OF 83 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 86148526 EMBASE

DOCUMENT NUMBER: 1986148526

TITLE: The effect of continuous subcutaneous insulin infusion therapy on morphological and biochemical abnormalities of peripheral nerves in experimental diabetes.

AUTHOR: McCallum K.N.C.; Sharma A.K.; Blanchard D.S.; et al.
 CORPORATE SOURCE: Department of Anatomy, University of Aberdeen, Marischal College, Aberdeen AB9 1AS, United Kingdom
 SOURCE: Journal of the Neurological Sciences, (1986) 74/1 (55-67).
 CODEN: JNSCAG
 COUNTRY: Netherlands
 DOCUMENT TYPE: Journal
 FILE SEGMENT: 037 Drug Literature Index
 003 Endocrinology
 008 Neurology and Neurosurgery
 005 General Pathology and Pathological Anatomy
 029 Clinical Biochemistry

LANGUAGE: English

AB Diabetes mellitus was induced in rats by the administration of streptozotocin and observations have been made over a period of 2 months in 3 groups of animals: controls, untreated diabetics and diabetics treated with continuous subcutaneous insulin infusion (CSII) therapy, using a 14-day Alzet osmotic minipump. Optimal control of day-to-day and 24-h blood glucose levels was achieved in diabetic animals treated with CSII. Body weight and skeletal growth, assessed by measurements of tibial length, were decreased in untreated diabetic rats and were normalized by insulin treatment. The concentrations of glucose, sorbitol and fructose in the nerves of diabetic animals were significantly increased and that of ***myoinositol*** significantly decreased; CSII therapy normalized these levels to those of age-matched controls. External myelinated fibre diameter in the tibial nerve was significantly less in untreated diabetic rats as compared with age-matched controls. In the insulin-treated group, fibre diameter significantly increased as compared with untreated diabetics and there was no significant difference between insulin-treated and control animals. Teased fibre preparations from the tibial nerve revealed very few abnormal fibres in all the three groups and no significant difference was detected between any of the groups. Continuous subcutaneous insulin infusion therapy, therefore, corrected biochemical abnormalities and also normalized myelinated fibre diameter in the peripheral nerves of experimental diabetic animals. The paradoxical excess of axonal degeneration that has been reported with conventional insulin treatment was not observed.

L9 ANSWER 72 OF 83 MEDLINE DUPLICATE 29
 ACCESSION NUMBER: 86059464 MEDLINE
 DOCUMENT NUMBER: 86059464 PubMed ID: 3877727
 TITLE: Characterization of responses of isolated rat hepatocytes
 to ATP and ADP.
 AUTHOR: Charest R; Blackmore P F; Exton J H
 SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1985 Dec 15) 260 (29)
 15789-94.
 Journal code: 2985121R. ISSN: 0021-9258.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 198601
 ENTRY DATE: Entered STN: 19900321
 Last Updated on STN: 19900321
 Entered Medline: 19860116

AB In isolated rat hepatocytes, ATP and ADP (10^{-6} M) rapidly mobilize intracellular Ca^{2+} and increase the concentration of free cytosolic Ca^{2+} ($[\text{Ca}^{2+}]_i$) within 1-2 s. The increase in $[\text{Ca}^{2+}]_i$ is maximal (2.5- to 3-fold) by about 10 s and is dose-dependent, with ATP and ADP being half-maximally effective at 8×10^{-7} and 3×10^{-7} M, respectively. At submaximal concentrations, the rise in $[\text{Ca}^{2+}]_i$ is transient due to hydrolysis of the agonist. The increase in $[\text{Ca}^{2+}]_i$ in response to ATP or ADP can be potentiated by low concentrations of glucagon (10^{-9} M). In addition, the $[\text{Ca}^{2+}]_i$ rise can be antagonized in a time- and dose-dependent manner by the ***tumor*** promoter 4 beta-phorbol 12 beta-myristate 13 alpha-acetate. Adenosine, at concentrations as high as 10^{-4} M, does not alter $[\text{Ca}^{2+}]_i$. AMP is ineffective at 10^{-5} M, but at 10^{-4} M it increases $[\text{Ca}^{2+}]_i$ approximately 1.5-fold after a 30-s lag and at a slow rate. Conversely, high concentrations (10^{-4} M) of adenosine and AMP increases cell cAMP about 2- to 3-fold. ATP and ADP, at concentrations (10^{-6} M) which near-maximally increase $[\text{Ca}^{2+}]_i$, do not affect hepatocyte cAMP. ATP and ADP increase the cellular level of ***myoinositol*** 1,4,5-trisphosphate (IP₃), the putative second messenger for Ca^{2+} mobilization. The increase in IP₃ is dose-dependent and precedes or is coincident with the $[\text{Ca}^{2+}]_i$ rise. There is an approximate 20% increase in IP₃ with concentrations of ATP or ADP which near-maximally induce other physiological responses. It is concluded that submicromolar concentrations of ATP and ADP mobilize intracellular Ca^{2+} and activate phosphorylase in hepatocytes due to generation of IP₃. These effects may involve P₂-purinergic receptors. In contrast adenosine and AMP interact with P₁ (A₂)-purinergic receptors to increase cAMP.

L9 ANSWER 73 OF 83 MEDLINE DUPLICATE 30
 ACCESSION NUMBER: 86033905 MEDLINE
 DOCUMENT NUMBER: 86033905 PubMed ID: 3932351
 TITLE: Stimulation of 1,2-diacylglycerol accumulation in
 hepatocytes by vasopressin, epinephrine, and angiotensin
 II.
 AUTHOR: Bocckino S B; Blackmore P F; Exton J H
 CONTRACT NUMBER: AM 33291 (NIADDK)
 SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1985 Nov 15) 260 (26)
 14201-7.
 Journal code: 2985121R. ISSN: 0021-9258.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 198512
 ENTRY DATE: Entered STN: 19900321
 Last Updated on STN: 19970203
 Entered Medline: 19851213

AB 1,2-Diacylglycerol (DAG) was measured in neutral lipid extracts from isolated hepatocytes using high pressure liquid chromatography followed by refractive index detection. Maximally effective doses of epinephrine, angiotensin II, and vasopressin increased DAG by approximately 65, 80, and

180-250%, respectively, with maximal increases being observed at 8-10 min. Depletion of cellular Ca^{2+} resulted in a 50% decrease in DAG accumulation elicited by vasopressin. Other agents which increased DAG levels were the ***tumor*** promoter 4 beta-phorbol 12 beta-myristate 13 alpha-acetate (120% increase at 10^{-6} M), the Ca^{2+} ionophore A23187 (385% increase at 10^{-5} M), and ATP (180% increase at 1 mM). The concentration dependence of DAG accumulation in response to epinephrine, angiotensin II, and vasopressin was similar to that found for ***myoinositol*** triphosphate accumulation (Chiarelli, R., Prpic, V., Exton, J. H., and Blackmore, P. F. (1985) *Biochem. J.* 227, 79-90), which was approximately 5-10 times less sensitive to hormone than was phosphorylase activation. Fatty acid analysis revealed that hormonally induced DAG was partially derived from sources other than inositol phospholipids. It is proposed from these studies that Ca^{2+} -mobilizing hormones elicit a prolonged increase in the levels of hepatocyte DAG, which may activate protein kinase C.

L9 ANSWER 74 OF 83 MEDLINE DUPLICATE 31
 ACCESSION NUMBER: 85282200 MEDLINE
 DOCUMENT NUMBER: 85282200 PubMed ID: 4027970
 TITLE: Metabolic fate of liposomal phosphatidylinositol in murine
 tumor cells: implications for the mechanism of
 tumor cell cytotoxicity.
 AUTHOR: Jett M; Chudzik J; Alving C R; Stanacev N Z
 SOURCE: CANCER RESEARCH, (1985 Oct) 45 (10) 4810-5.
 Journal code: 2984705R. ISSN: 0008-5472.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 198510
 ENTRY DATE: Entered STN: 19900320
 Last Updated on STN: 19980206
 Entered Medline: 19851023

AB The mechanism of the previously reported cytotoxicity of liposomes containing plant phosphatidylinositol (PI) against numerous ***tumor*** cell lines was examined in detail by using liposomes containing synthetic PI specifically labeled either with radioactive myo-inositol, or in the sn-2 position with radioactive linoleic acid, oleic acid, or arachidonic acid. The uptake of liposomal PI by N4TG1 neuroblastoma cells increased with time and was dependent on the nature of the fatty acids. Uptake was highest with liposomal PI containing linoleic acid followed by arachidonic acid and then by oleic acid. The cellular fate of liposomal PI was determined by analysis of radioactive metabolites present in extracts of ***tumor*** cell lipids. Appearance of liposomal PI metabolic products in the ***tumor*** cells was correlated with thymidine uptake as a measure of viability. After 3 h incubation of cells with PI liposomes it was found that the release of both radioactive liposomal fatty acids (and probably also lyso-PI) and radioactive diglycerides was correlated inversely with the cellular uptake of [methyl-3H]thymidine and uptake of [3H] ***myoinositol***. An experiment in which liposomes were prepared both from animal PI which contained predominantly saturated fatty acids in the sn-2 position and an increasing mole fraction of a synthetic PI containing radioactive linoleic acid in the sn-2 position established that the amount of PI containing linoleic acid in the sn-2 position could be correlated with a decrease in the amount of thymidine uptake by ***tumor*** cells. The above results clearly established that phospholipases A2 and C in the ***tumor*** cells were responsible for the formation of metabolites of liposomal PI, and these metabolic products might have been responsible for cytotoxicity and cell death.

L9 ANSWER 75 OF 83 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 1985:576367 CAPLUS
 DOCUMENT NUMBER: 103:176367
 TITLE: Saccharide excretion from rats with lymphomas
 AUTHOR(S): Meagher, R. B.; Furst, S. J.; Furst, A.
 CORPORATE SOURCE: Inst. Chem. Biol., Univ. San Francisco, San Francisco,

CA, 94117-1080, USA

SOURCE: Proceedings of the Western Pharmacology Society
(1985), 28, 331-3
CODEN: PWPSA8; ISSN: 0083-8969

DOCUMENT TYPE: Journal

LANGUAGE: English

AB As rats with lymphomas became moribund, urine glycerol levels and most carbohydrate levels decreased compared to normal controls. However, glucose, galactose, and sucrose increased. The inverse levels of glucose and glycerol may reflect the degree of oxidn. of glucose. During development of the tumors, fructose, mannose, glucose, galactose, mannoheptulose, sucrose, and ***myoinositol*** increased. Urea was the major excretion product for both the exptl. rats and controls; however, urea excretion was lower in the ***tumor*** -bearing rats. A group of rats within the control group, which excreted high amts. of glucose, were termed diabetic, and their saccharide excretion was also monitored.

L9 ANSWER 76 OF 83 MEDLINE DUPLICATE 32

ACCESSION NUMBER: 78084382 MEDLINE

DOCUMENT NUMBER: 78084382 PubMed ID: 202462

TITLE: Quantitative determination of ***myoinositol***, inositol 1-phosphate, inositol cyclic 1 : 2-phosphate and glycerylphosphoinositol in normal and Rous-sarcoma-virus-transformed quail fibroblasts under different growth conditions.

AUTHOR: Diringer H; Koch-Kallnbach M E; Friis R R

SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, (1977 Dec) 81 (3) 551-5.
Journal code: 0107600. ISSN: 0014-2956.

PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 197803

ENTRY DATE: Entered STN: 19900314

Last Updated on STN: 19970203

Entered Medline: 19780321

AB ***Myoinositol*** and its phosphorylated derivatives have been quantitatively determined in normal and Rous-sarcoma-virus-transformed quail cells under various growth conditions using [2-(3)H] ***myoinositol*** at isotope equilibrium conditions. The following amounts were determined (nmol/mumol phospholipid, as a unit of cell mass): exponentially growing normal and ***tumor*** cells contained 25-40 nmol free inositol, 0.40-0.45 nmol ***myoinositol*** 1-phosphate, 0.30-0.50 nmol glycerylphosphoinositol, and 0.03-0.04 nmol ***myoinositol*** cyclic 1 : 2-phosphate. At high cell populations in the absence of serum, conditions which result in cessation of growth by normal but not by ***tumor*** cells, changed levels were found for glycerylphosphoinositol and free inositol. In ***tumor*** cells the levels of these two compounds increased to 0.64 nmol and 64 nmol, respectively. In normal cells glycerylphosphoinositol increased to 0.95 nmol and free inositol showed highly elevated levels of 144 nmol. At short pulses the specific activities of inositol 1-phosphate and inositol cyclic 1 : 2-phosphate were found to be higher than that of phosphatidylinositol. This was not the case for glycerylphosphoinositol.

L9 ANSWER 77 OF 83 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 78099138 EMBASE

DOCUMENT NUMBER: 1978099138

TITLE: Accumulation of materials by a papilloma of the choroid plexus in vitro.

AUTHOR: Spector R.; Lorenzo A.V.; Welch K.

CORPORATE SOURCE: Dept. Neurosci., Child. Hosp. Med. Cent., Boston, Mass.
02115, United States

SOURCE: Developmental Medicine and Child Neurology, (1977) 19/3
(388-391).

CODEN: DMCNAW

COUNTRY: United Kingdom
 DOCUMENT TYPE: Journal
 FILE SEGMENT: 008 Neurology and Neurosurgery
 005 General Pathology and Pathological Anatomy
 007 Pediatrics and Pediatric Surgery
 030 Pharmacology

LANGUAGE: English

AB A large papilloma, presenting in a newborn child and showing, in its history, features of malignancy, was studied by incubating fragments in a gaseous nutrient solution to which one of several substrates had been added. Folic acid, ***myoinositol***, scyllitol and leucine were weakly accumulated, so that the concentration in the tissue was greater than in the bath. Penicillin entered the tissue by a saturable mechanism, but the concentration in the tissue was not greater than in the surrounding solution. Iodide was not accumulated. Microscopically, the papilloma, although malignant, was easily recognized as choroid plexus. Even though large portions of the papilloma appeared to be necrotic on examination, a portion was viable, as evidenced by the ability of the ***tumor*** to accumulate leucine and incorporate it into macromolecules.

L9 ANSWER 78 OF 83 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1973:70043 CAPLUS

DOCUMENT NUMBER: 78:70043

TITLE: Effect of myo-inositol on the induction of
 experimental allergic encephalomyelitis in guinea pigs

AUTHOR(S): Tsumita, Toru; Saito, Michiko; Nagai, Yoshitaka

CORPORATE SOURCE: Inst. Med. Sci., Univ. Tokyo, Tokyo, Japan

SOURCE: Japanese Journal of Experimental Medicine (1972),

42(6), 587-8

CODEN: JJEMAG; ISSN: 0021-5031

DOCUMENT TYPE: Journal

LANGUAGE: English

AB ***Tumor***-specific cell surface structure(s) may be masked or covered with myo-inositol, leading to a decrease in the response of the host. To confirm the effect of myo-inositol on the modification of antigenicity, an expt. was carried out by employing an induction system of exptl. allergic encephalomyelitis (EAE). Two groups of guinea pigs which received EAE antigen alone, 100 .mu.g and 50 .mu.g, showed typical symptoms of EAE, body wt. loss, and paralysis and died within 2-2.5 weeks. The lethal rate was 100%. However, the exptl. groups which received the antigen mixed with myo-inositol showed lower mortality than that of the control group. For 50 .mu.g of the antigen and 2.0 mg of myo-inositol, the rate was only 25%. Some animals showed paralysis, but recovered during the observation period (40 days). scyllo-Inositol was also effective. Mannitol was less active than these cyclitols.

L9 ANSWER 79 OF 83 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1973:69901 CAPLUS

DOCUMENT NUMBER: 78:69901

TITLE: ***Tumor*** host relation. V. Effect of
 myo-inositol on ***tumor*** cell growth in vivo
 and on the resistant activity of the host

AUTHOR(S): Tanino, Takae; Narumi, Koyu; Tsumita, Toru

CORPORATE SOURCE: Inst. Med. Sci., Univ. Tokyo, Tokyo, Japan

SOURCE: Japanese Journal of Experimental Medicine (1972),

42(6), 575-82

CODEN: JJEMAG; ISSN: 0021-5031

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In a syngenic mouse ascites ***tumor*** system (C3H/He mouse and MM2 mammary carcinoma cells) i.p. injections of myo-inositol (10 mg/mouse, 7 alternate days) enhanced the growth of ***tumor*** cells. The ***tumor***-bearing mice died sooner than untreated mice. The no. of ***tumor*** cells increased 50% more and the mitotic ***tumor*** cells were found 2.5-3 times more frequently than in the untreated case. Survival rate of the mice after removal of ***tumor*** cells was lower

than that of control mice. The titer of ***tumor*** cell growth inhibition activity of the serum and of the spleen cells decreased significantly.

L9 ANSWER 80 OF 83 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1968:11030 CAPLUS

DOCUMENT NUMBER: 68:11030

TITLE: Transport of ***myoinositol*** in Ehrlich ascites cells

AUTHOR(S): Johnstone, Rose M.; Sung, Cheng-Po

CORPORATE SOURCE: McGill Univ., Montreal, Can.

SOURCE: Biochimica et Biophysica Acta (1967), 135(5), 1052-5

CODEN: BBACAQ; ISSN: 0006-3002

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Ehrlich ascites cells can transport and accumulate inositol by an energy-, Na⁺-, and K⁺-dependent process which is unable to undergo exchange diffusion. Thus, when suspensions of the cells were incubated with ***myoinositol*** -14C (I), there was extensive accumulation of 14C in the tissue. Anaerobically, glucose was required for accumulation, while aerobically it was not required. Accumulation was greatest in a bicarbonate medium contg. glucose. It could be inhibited by removal of Na⁺ or K⁺ or by addn. of 2,4-dinitrophenol. I was taken up only slowly by the ascites cells, and once inside the cells, the rate of loss of I to a medium free of I was also slow. A 10-fold increase in the apparent Km value for I uptake was observed when most of the Na⁺ of the medium was replaced by isomolar sucrose; the max. uptake of I was not changed. I did not appear to undergo exchange diffusion; no exchange was detected in either sucrose or normal Ringer medium, despite the increase in apparent Km in a Na⁺-deficient medium. In a sucrose medium, however, an increased loss of 14C from the tissue was noted after 20 min. of incubation.

L9 ANSWER 81 OF 83 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1963:457457 CAPLUS

DOCUMENT NUMBER: 59:57457

ORIGINAL REFERENCE NO.: 59:10588b-c

TITLE: Failure of 10 congeners of myo-inositol to support or to inhibit the growth of a cultured human cell

AUTHOR(S): Eagle, H.; McCasland, G. E.

CORPORATE SOURCE: Albert Einstein Coll. of Med., New York, NY

SOURCE: Biochemistry (1963), 2(5), 1125-6

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB Ten congeners of myo-inositol failed to support the growth of a human ***cancer*** cell (KB) even at 10-4 g./ml., 1000 times the min. effective concn of ***myoinositol*** itself. Eight compds. tested at 10-3 g./ml. failed to inhibit the growth-promoting activity of myo-inositol at 2 .times. 10-6 g./ml., a ratio of analog to myo-inositol of 500:1.

L9 ANSWER 82 OF 83 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1961:60554 CAPLUS

DOCUMENT NUMBER: 55:60554

ORIGINAL REFERENCE NO.: 55:11610e-f

TITLE: Anemia-inducing substances from stomach ***cancer*** tissue. I. On a dialyzable active substance

AUTHOR(S): Masamune, Hajime; Kawasaki, Hiroya; Shinohara, Hyogo

CORPORATE SOURCE: Tohoku Univ., Sendai

SOURCE: Tohoku J. Exptl. Med. (1960), 72, 348-55

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB Dialyzed exts. of human gastric carcinoma yielded a substance identified as ***myoinositol*** which produced anemia when injected intravenously in rabbits. This, as well as a com. sample of ***myoinositol***, induced a 10-15% drop in circulating erythrocytes 5 hrs. after injection of 0.2 mg./kg. It was also isolated in high yield from normal gastric mucosa.

L9 ANSWER 83 OF 83 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1976:206916 BIOSIS

DOCUMENT NUMBER: BA62:36916

TITLE: VITAMINS AND HORMONES ADVANCES IN RESEARCH AND APPLICATIONS
VOL 33.

AUTHOR(S): MUNSON P L; ET AL.

SOURCE: VITAM HORM, 1975 (RECD 1976), 743.

CODEN: VIHOAQ. ISSN: 0083-6729.

DOCUMENT TYPE: Book; Conference

FILE SEGMENT: BA; OLD

LANGUAGE: Unavailable

AB Contributions to the symposium on endocrine control of the prostate comprise the 1st part of this volume. Hormonal effects on prostate cell proliferation, androgen effects on rat ventral prostate, prostatic polynucleotide polymerase reactions, animal models in antiprostatic drug studies, test systems for chemotherapeutic agents, prostate production of testosterone, androgen binding and metabolism, androgens in testis and epididymis, androgen receptors and their hormonal control, estrogenic treatment of prostatic carcinoma, management of reactivated prostatic ***cancer***, androgen metabolism in benign prostatic hypertrophy, and nonsurgical treatment of benign prostatic hypertrophy are among the areas covered. The 2nd part of this volume contains papers on thiaminases, amino acid imbalance in pellagra, ***myoinositol*** lipids, steroid hormone receptors and hormonal control of cartilage growth and metabolism. Individual articles are indexed in BIORESEARCH INDEX.

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(FILE 'HOME' ENTERED AT 13:53:10 ON 17 JAN 2003)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 13:53:23 ON 17 JAN 2003

L1 71 S INOSITOLPHOSPHOGLYCAN
L2 3020983 S CANCER OR TUMOR OR TUMOUR
L3 6 S L1 AND L2
L4 3 DUP REM L3 (3 DUPLICATES REMOVED)
L5 4165 S MYOINOSITOL
L6 145 S L5 AND L2
L7 80 DUP REM L6 (65 DUPLICATES REMOVED)
L8 151 S L6 OR L3
L9 83 DUP REM L8 (68 DUPLICATES REMOVED)